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Blood Pressure Management in Frail Older People - The Real World Experience

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Blood Pressure Management in Frail Older People - The Real World Experience

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Abstract- According to recent evidence, blood pressure (BP) management benefits the same patients with mild frailty and fit subjects. In contrast, there is no evidence that antihypertensive treatment benefits patients with severe frailty, yet much evidence that such treatment is not safe. Notably, comorbidities can impact on benefits and harms of BP treatment. For enabling patient management based on individualized expected outcomes, there is a need to substantially increase observational data, focused on complex clinical situations and various comorbidities. In line with this aim, we present our experience from the perspective of long-term geriatric care. It is hoped that observations from the bedside, enhanced and expanded in the future, might contribute to the shift from empirical practice towards an evidence-balanced approach.

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I. INTRODUCTION

Lowering the blood pressure (BP) in the elderly confers cardiovascular benefits, as was documented in SHEP, Syst-Eur, HYVET, and SPRINT (1-3). However, as shown in the regards cohort, in longstanding hypertension there may be a point of lesser return or no return. (4). With longstanding hypertension, this residual atherosclerotic damage becomes a prevailing risk factor, and hemodynamic normalization of BP confers less benefit (5). Guidelines of arterial hypertension treatment are not available for frail older people, but recent evidence indicates that BP management in patients with mild frailty should not differ from BP management in fit subjects (2). However, concerning patients with severe frailty there is no evidence that antihypertensive treatment reduces cardiovascular events, but much evidence that such treatment is not safe (6, 7). In recognizing that high BP in older adults is a complex and heterogeneous condition, the Report of the American College of Cardiology / American Heart Association Task Force on Clinical Practice Guidelines 2017 (8) makes a distinction between BP goals appropriate for fit patients and BP goals in hypertensive elderly subjects having a high burden of comorbidity and limited life expectancy. In the latter, clinical judgment and patient preference should be the basis of management. Indeed, achieving BP < 130 / 80 mm Hg may not be feasible in some older

patients (5). Not uncommonly, these patients experience dizziness and poor cognition when systolic BP hovers below 140 mm Hg. For now, over treated hypertension appears to be prevalent in nursing home patients.

a) Blood Pressure Measurement - Points Deserving Emphasis

Mercury sphygmomanometry has for long been the gold standard for BP measurement. However, mercury sphygmomanometers in the main have mostly been replaced with automatic devices. Oscillometric BP devices detect the motion of the BP cuff transmitted from the underlying artery, but the transmitted oscillations also depend on the arteries' stiffness and may be disturbed by low-frequency mechanical vibration originating in the environment. Oscillometric BP measurements may be patient dependent: hence, a disagreement between oscillometric BP and sphygmomanometric measurement may vary from patient to patient. Oscillometric BP measurements also are device dependent, because the algorithms used to compute the BP differ from one device to the other. An inconsistency of measurements by the same device and in the same patient may exist. A device passing a validation test does not mean that accurate readings in all patients will be achieved (9).

Clinic BP measurements alone to detect hypertension result in about 20% false-positive diagnoses due to the white-coat effect. The accuracy of office BP measurement can be improved by using a specially programmed electronic sphygmomanometer, capable of recording automatically, with the patient resting quietly and alone, an initial test reading followed by five additional readings at one or more minutes apart. There is evidence to support the replacement of manual office BP measurement with a such specially programmed automated BP device (e.g., the BpTRU), which is more accurate and not subject to a white coat response (10, 11). Twenty-four-hour ambulatory BP monitoring is the ideal method of diagnosing white-coat hypertension as well as masked hypertension. Concordance between office and ambulatory BP values is imperfect in nursing home residents, yet, this disparity appears to be unimportant in practice since one year survival of residents is predicted more accurately by disability than by BP (12). In long-term geriatric care, use of an automated BP device with multiple recordings on a single visit might serve as a more affordable alternative to 24-hour ambulatory BP monitoring (13).

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BP measurement may entail inaccuracies, some of which should be avoided: inappropriate cuff size; presence of arrhythmias causing the BP to be highly variable - multiple readings are needed to increase accuracy; unexposed inter-arm BP differences; missing the diagnosis of orthostatic hypotension when all measurements are obtained with the patient supine; missing the diagnosis of supine hypertension when all measurements are taken with the patient sitting; unawareness of hypotension during an acute febrile illness when medications need to be tapered down; BP overshoot after recovery from acute illness, when up-titration of antihypertensive medications may be required (14). Guidelines advise that the BP be measured on both arms, a recommendation often ignored. Measurement in only one arm may lead to underdiagnosis of hypertension. In practice, there should be awareness of the inherent limitations of automatic BP devices, of possible errors in measurement. Unlikely results need to be confirmed and interpreted within the clinical context, as illustrated by the following incident.

A 70-year-old woman was the first patient in a pilot study that aimed to assess the frequency of orthostatic hypotension (OH) and postprandial hypotension (PPH) in a population of severely frail patients. She was previously diagnosed with arterial hypertension and diabetes mellitus. Recently she suffered a minor stroke. At the time of admission for post-acute care, the patient's supine BP was 90-100/40 while being treated with three antihypertensive medications. Multiple BP measurements were recorded in the sitting patient with an automatic device by a physician, in conformity with the study protocol (Table 1). Along the measurements, the patient was awake and comfortable.

Table 1: Large Inter-Arm BP Difference, Unsuspected

Time	Relative to Lunch	Arm	SBP	DBP	HR
12.00	Before	Left	76	37	75
			76	43	72
			71	40	69
12.05		Right	115	48	72
			113	32	69
			117	48	70
13.05	After*	Right	128	53	72
			124	56	71
			120	55	71

*Lunch composition: total 480 Kcal, carbohydrates 250 Kcal, proteins 95 Kcal, lipids 135 Kcal

In recognizing a wide inter-arm BP difference in this patient, measurements were required to be done on the right arm (the arm with the higher BP): antihypertensive medications were titrated accordingly. This episode is a reminder to the recommendation, often ignored, that the BP should be measured on both

arms. The prevalence of systolic inter-arm difference of BP >10 mm Hg in the general population ranges from 14% to 23.6% and several reports show no association with age. An inter-arm SBP difference ≥ 10 mmHg is associated with increased cardiovascular risk and a difference ≥ 15 mm Hg with an increased cerebrovascular risk (15). Measurement in one arm only, by chance with the lower BP, may lead to underdiagnosis or under treatment of hypertension.

The method of BP measurement is particularly important when determining the patients' BP goal. However, proper BP assessment is time-consuming. The consequence of inappropriate BP measurement may be that many people, labeled as patients with hypertension, receive pharmacologic therapy that is unlikely to provide benefit but may cause adverse events.

b) Diagnosing Arterial Hypertension

Arterial hypertension has been defined as usual systolic BP ≥ 140 mmHg and/or usual diastolic BP ≥ 90 mmHg. Above these BP levels, the benefits of antihypertensive pharmacological treatment have been established in randomized placebo-controlled trials (16). So defined, arterial hypertension affects one-fourth of the adult population: by 75 years of age, almost 90% of the people will have hypertension. Typically, patients who develop hypertension before the age of 50 years have combined systolic and diastolic hypertension, in which the main hemodynamic alteration is vasoconstriction at the level of resistance arterioles. Most patients who develop hypertension after the age of 50 years have isolated systolic hypertension, the primary abnormality being decreased distensibility of the large conduit arteries. Yet, in the oldest old, declining systolic BP is common. The GERDA cohort study provided longitudinal data on participants aged 85, 90, and ≥ 95 years from 2000 to 2015. The mean change in systolic BP was by -12 mmHg (SD -25) and was explained by deteriorating general health (17).

More restrictive BP categories have been proposed in recent guidelines: normal BP <120/80 mmHg, elevated BP 120-129/<80 mmHg, stage 1 hypertension BP 130-139/80-89 mmHg, stage 2 hypertension BP $\geq 140/90$ mmHg (8). The new guidelines focus on proper BP measurement and encourage home BP monitoring. Based on the SPRINT study as well as the new guidelines (8), more aggressive treatment goals are recommended in the highest-risk patients. Concerning older adults, it can be assumed that the vast majority have a 10-year ASCVD risk $\geq 10\%$, placing them in the high-risk category that requires initiation of antihypertensive drug therapy at BP $\geq 130/80$ mm Hg. In practice, there are reservations concerning the application of the lower threshold for hypertension diagnosis. In many older persons treating hypertension to goal BP according to the new guidelines may be

problematic, in particular in patients with numerous comorbidities and severe frailty (18).

c) *Hypertension and Frailty - The Blood Pressure Paradox in the Oldest Old*

There is scarce information about the prevalence of arterial hypertension among frail elderly patients. A cross-sectional study conducted on 619 older adults at a university-based outpatient center evaluated the prevalence of hypertension in the robust, prefrail, and frail elderly. Hypertension was more prevalent in the frail (83%) and prefrail (72.5%) groups than among controls (51.7%). Hypertension, physical activity, the number of prescribed drugs, and the cognitive performance were significantly associated with frailty status (19). A study from South Korea (20) analyzed data of 4,352 adults aged ≥ 65 years, among them 62.0% had hypertension and 21.3% had pre-hypertension. Hypertension prevalence was higher in frail elderly (67.8%) than in pre-frail (60.8%) or robust elderly (49.2%). It was suggested that intensive control of hypertension could influence the trajectory of frailty (15): a hypothesis that needs more substantiation (19).

A cross-sectional study in four nursing homes included 480 longterm residents, all Caucasian (Naschitz JE et al., presented at the meeting of the Israel Hypertension Society). Their average age was 83.2 years, 56% were women, the average CSHA frailty index was 6.1. A requirement for being included in the study was the patients being clinically stable during the current month. Excluded were bedridden persons. Oscillometric measurements at the arm level were recorded with a standard automated BP cuff system, Welch Allyn Spot Vital Signs, San Diego, USA. This model achieved a British Hypertension Society grade A for both SBP DBP: it also met the criteria for the Advancement of Medical Instrumentation protocol. The medians of sitting BP measurements recorded during the current month were analyzed and related to the intensity of antihypertensive treatment. The SBP average was 124.9 (SD 12.4), SBP median 125 mmHg. The DBP average was 70.5 (SD 7.2), median DBP 70 mmHg. Fifty-three percent of the patients were not receiving BP-lowering medications. For those receiving antihypertensive medications (about 2/3 were taking ramipril 2.5 mg/day), the mean 'intensity of antihypertensive treatment' (21) was 0.6, i.e., low doses and unexpected good response. There were infrequent OH or orthostatic symptoms, as all subjects were symptom-free on sitting for 3-4 hours. All enjoyed daily 15-20 minutes of assisted walk.

In two subgroups, 39 fallers and 102 without a history of falls during the preceding six months, the sitting BP variability was computed based on all sitting BP measurements recorded during the preceding six months. The standard deviation (SD) of the BP values in each subject was used as a measure of BP variability. A low visit-to-visit BP variability was found in both

subgroups (SBP SD 8.9 mmHg and 8.9 mmHg, respectively) in comparison to other studies. In the PROSPER study of elderly at risk the SD of the SBP was 14.4 mmHg: in the ASCOT-BPLA study the visit-to-visit SD of the SBP was 10.66 mmHg in amlodipine treated patients and 13.4 mmHg in atenolol-treated patients: in ALHAT the values were SBP SD 10.6, 10.5, and 12.2 for participants randomized to chlorthalidone, amlodipine, and lisinopril (22-24).

Remarkable and contrary to expectation were the normal SBP, normal DBP and normal PP (or normalized on treatment) in a population of old persons, the 'favorable' BP variability, and the tolerance to orthostatic challenges of daily life. The interpretation of this data is speculative, but for could be attributed to the survivor effect similar o the decreased prevalence of cardiovascular disease observed in patients above 85 years. Indeed, it is reasonable to assume that patients who survived the longest were the least likely to be afflicted by these conditions (25). In expressing our surprise relative to the observed and being short of understanding, we used to call this phenomenon "the blood pressure paradox of the frail oldest old."

d) *BP Goals for Older Adults with a High Burden of Comorbidity and Limited Life Expectancy*

Patients with frequent falls, advanced cognitive impairment, multiple comorbidities and limited life expectancy may be at risk of adverse outcomes with intensive BP lowering. Evidence-based recommendations for BP management in the latter are not available since persons presenting any of these conditions were not included in large RCTs focused on hypertension treatment.

The "J-side" of BP lowering: Vital organs may respond differently to BP lowering. While decreasing the BP to the proposed target may reduce the incidence of stroke and end-stage renal disease, any protective effect on coronary events may be nil or even reverted with low BP. Caution is needed in patients with severe organ impairment, with a recent cardiovascular event and in the old, in whom vital organs may be more affected by under perfusion related to a treatment-induced BP fall (26,27). A diastolic BP level of less than 60 mm Hg should be avoided due to the potential for an increase in cardiovascular risk (28). Whether diastolic BP <70 mmHg along with high pulse pressure and OH are independent risk predictors for vascular events, and whether their association with frailty increases the risk needs to be addressed in further studies.

Injurious falls on antihypertensive treatment: In examining the relationship between antihypertensive therapy, the achieved BP, frailty indicators, and Medicare claims for injurious falls, it was shown that neither on-treatment BP nor the number of classes of antihypertensive medications used was associated with injurious falls: yet, having more than one frailty indicator

was associated with falls. Thus, fear of injurious falls should not be an obstacle in prescribing antihypertensive therapy when deemed necessary. Frailty, on the contrary, especially when multi-dimensional, constitute a warning sign (29, 30).

The optimum age-related SBP in the 75+ old that was predictive of the lowest cardiovascular and 10-year mortality has been observed in the systolic BP range 140-179 mmHg. It appears that a moderately elevated BP might be a favorable augur in those aged >80years (31). A possible explanation to this observation may be a disturbance of regulatory mechanisms involved in the perfusion of vital organs: so, an elevated BP might act as a compensatory mechanism in the oldest old to preserve organ perfusion and prevent organ damage.

Disordered cerebral blood flow autoregulation: Autoregulation of the cerebral blood flow is a protective mechanism that maintains flow at a relatively constant level despite fluctuations of arterial BP. In general, a brachial mean BP ≥ 60 mmHg is thought to afford an adequate cerebral blood flow. Cerebral blood flow autoregulation may be affected by a diversity of physiologic and pathological conditions (32-36): advanced age, endotheliopathy, hypertension, diabetes mellitus, heart failure, hypocapnia, alkalosis, sympathetic arousal, autonomic failure, early after head injury, acute ischemic stroke or sepsis. The cerebral flow reserve also depends on the presence of cerebral small and large artery disease. A focal decrease of cerebral flow may cause transient ischemic events, subcortical infarctions, cognitive decline, while a global decrease may cause presyncope or syncope.

Hypotension induced by medication, dehydration or sepsis may trigger ischemic cerebrovascular or coronary events (37-39).

Orthostatic hypotension (OH) and postprandial hypotension (PPH) are common disorders which accumulate with age. OH is defined as a sustained reduction of either systolic BP by ≥ 20 mmHg or diastolic BP by ≥ 10 mmHg within 3 minutes of standing or on passive head-up tilt to at least 60° (40). Some patients have 'delayed OH' that occurs beyond 3 minutes of standing. The prevalence of OH may be as high as 30-50 % among residents in long-term geriatric care (41,42). OH may concur with dizziness, falls and frailty, and has been regarded as a major cause of morbidity. Despite a large fall in BP, patients with OH often are asymptomatic, i.e., OH unawareness. The latter is explained by efficient regulation of the cerebral blood flow, so the cerebral blood flow does not change within a large range of the systemic BP. In patients with chronic OH, the tolerance to low BP may expand as low as systolic BP 70 mmHg (43). Symptom-free OH has been described in patients with dementia (44) and also in 75% of a population with autonomic failure (45). OH in older people has been considered an omen of death

(46), but adjusted for frailty OH's impact on mortality was not significant (47, 48).

Postprandial hypotension (PPH) is defined as a decrease in systolic BP of at least 20 mmHg within two hours after a meal (49). PPH, like OH, is thought to be a major cause of morbidity in older people (50). Nearly all older persons living in nursing homes experience some postprandial decrease in BP, usually not meeting criteria for diagnosing PPH. The possibility of PPH should be considered in patients with syncope, falls and dizziness that occur within two hours after a meal. For diagnosing PPH, experts recommend that the patient have both postprandial symptoms and a postprandial BP decrease. It is considered a good practice that symptomatic patients undergo ambulatory BP monitoring with analysis of breakfast and lunch hemodynamics (49). Alternatively, precisely timed small numbers of measurements may be valuable with monitoring the BP and symptoms for 2 hours after a meal since the nadir in BP can occur as late as 2 hours postprandially (51).

Three tests are widely used for the diagnosis of OH: the supine-to-standing orthostatic test, the supine-to-sitting, and the head-up tilt test.

The supine-to-standing orthostatic test is frequently used according to the following protocol: the patient's brachial BP is measured after 5-10 minutes of rest in the supine position: then the patient stands up and measurements are repeated while the patient stands motionless for 3-5 minutes with the cuffed arm supported at heart level. While standing, the patient is asked to report dizziness or light-headedness, with the examiner recording the symptoms' transience or persistence. The procedure is aborted for safety reasons if the BP drops precipitously or presyncope ensues. Patients with severe autonomic failure have an immediate drop in BP on standing and OH is easily diagnosed. On the other hand, there are individuals in whom the onset of hypotension on standing is delayed, and the diagnosis is missed using the short orthostatic test (52,53). The methodology of the supine-to-sitting orthostatic test is not standardized. One protocol often used involves a single BP measurement supine after prolonged recumbence followed by BP measurements after 1, 3 and 5 minutes of sitting. Other technical details are similar to those of the supine-to-standing test.

Reproducibility of cardiovascular responses on orthostatic challenge has been inconsistent (55, 55). OH was most prevalent and severe in the morning when subjects first arose: hence, OH may be underestimated when testing is performed in the afternoon (54). An influence of meals on the diurnal variation of OH has been observed.

e) *Screening Residents of Nursing Homes for OH and PPH Necessary?*

Frail older people have not been systematically assessed for OH and PPH. In a study from our

institution, we assessed BP changes related to posture and meals in frail older patients. The patient population comprised 50 older people, resident in long-term geriatric or hospice care, who were severely frail, ADL dependent, bed and chair confined, feeding orally. They were unfit to undergo standard postural and prandial tests, and unable to comply with ambulatory 24-hour-BP recording or beat-to-beat BP monitoring. The CSHA Clinical Frailty Scale (56) was used to estimate frailty severity, in which score 6 is the label for moderately frail persons needing help with both ADL and IADL and 7 indicates complete dependence. The average CSFA in the study population was 6.6 (SD 0.32). Excluded were patients not fully alert and those affected by an intercurrent illness such as febrile states, diarrhea, severe acute pain, exacerbation of dyspnea, and acute renal failure. The defining outcome of the study was postural fitness under real-life conditions rather than results of postural and prandial laboratory tests.

The brachial BP and HR were measured at heart level with a Spot Vital Signs® validated automatic oscillometric device. Supine BP and HR were recorded by a nurse at the bedside at 7 a.m.: for analysis, measurements taken over the previous ten days were used, including the measurement on the test day. Sitting BP and HR before lunch at 12 a.m. were measured on test day by a physician after the patients had been sitting in the dining room for 30-120 minutes. Three to five measurements were acquired, scrutinized for artifacts in real time, and discarded when found. Sitting BP and HR after lunch, in the dining room, at 12.40-13.00 a.m., were determined by the same physician. The medians of 3-5 measurements - supine, sitting before lunch and sitting after lunch - were chosen for analysis. Patient alertness and incident symptoms were assessed shortly before lunch and shortly after lunch. Incident symptoms were recorded, including dizziness, fatigue, lightheadedness, visual impairment, headache, chest pain, and pain in the shoulders or neck. Shortly after lunch, the patients were returned to their beds. Incident symptoms during the subsequent two hours were followed by nurses. Primary outcome measures of our study were the number of tests discontinued and incident symptoms occurring during the tests. Secondary outcome measures were incident OH (OH equivalent), incident PPH (PPH equivalent), and mean BP <60 mmHg at any time during the test. A BP drop to a magnitude, which on standard testing is diagnosed OH, by the present protocol was called 'OH equivalent.' We used the label 'PPH equivalent' to indicate a BP drop that under standard conditions (51) would be called PPH. The latter was correlated with the caloric content of the lunch consumed. The differences between supine BP and sitting before lunch BP were used to diagnose OH. Differences between sitting before lunch SBP and sitting after lunch SBP were used to diagnose PPH. During a four month period, 48 consecutive patients

fitting the inclusion criteria were evaluated once or twice. Their average age was 79.4 years (SD 10 years), with 22 males and 28 females. Results of measurements are shown in Tables 2 and 3. In no instance was the mean BP less than 60 mmHg. During a 2-16 months of hospitalization, there were neither falls, syncope, stroke, nor acute coronary events in the study population.

Table 2: Blood Pressure Measurements Supine and Sitting, Before and After Lunch

Parameter	Supine	Sitting Before Lunch	Sitting After Lunch
SBP mmHg, Mean (SD)	121.2 (16.8)	118.2 (19.1)	117.2 (20.9)
DBP mmHg, Mean (SD)	67.7 (10.5)	62.5 (10)	61.5 (9.9)
Heart Rate, Mean (SD)	80.8 (13.7)	76.8 (12.8)	79.6 (13.9)

Table 3: Number of Tests Exhibiting OH and PPH (Equivalents)

BP Change	Supine to Sitting Before Lunch	Sitting Before Lunch to Sitting After Lunch
A. SBP Decrease by $\geq$ 20 mmHg	9	8
B. DBP Decrease by $\geq$ 10 mmHg	16	4
A and / or B	23	8

In general, a brachial mean BP $\geq$ 60 mmHg (63/63 tests in the present study) is considered satisfactory to provide adequate cerebral blood flow. However, the situation may early after head injury or an acute ischemic stroke when autoregulation of the cerebral blood flow may be altered, and the brain remains unprotected against BP changes. Cerebral blood flow autoregulation may also be compromised during sepsis, potentially resulting in brain damage (36). No patient in our study belonged to either category mentioned above. In patients with severe frailty, there is no proof that diagnosis of asymptomatic OH and PPH improves the clinical outcomes (57,58). On the other hand, when symptoms of low cerebral perfusion occur, an appropriately elaborate work-up and treatment should be implemented.

The routine of residents sitting and eating in the dining room is always preferred to isolation and being bed-bound. In observing that severely frail older people tolerated the postural and prandial challenges to which they had been habitually exposed, the message could be that systematic screening residents for OH and PPH might be unnecessary and avoidable.

f) Deintensification of Antihypertensive Treatment

Little is known about deintensification of antihypertensive treatment in elderly hypertensives (59), in general, and so in the particular case of severely frail older people. A retrospective pilot study from a long-term comprehensive nursing institution addressed severely frail residents (Naschitz et al., unpublished observations). Included were 24 previously diagnosed hypertensives who were clinically stable for at least three months, not contracting any inter current disease. There were 13 males and 11 females: their mean age was 72.8 years (SD 14.9), their frailty severity 6 or 7 according to the CSHA Clinical Frailty Scale. The BP was recorded with a validated automatic BP device in supine position. Measurements obtained one month after admission, the time considered adequate for accommodation in the new surrounding, were compared with measurements obtained 3 months later. The median of all readings, 5 or more, obtained over 10-14 days was calculated for each of the two time periods. The number of different antihypertensive medications was counted and the intensity of antihypertensive treatment was calculated for each period (21). In being a retrospective analysis, adjustments of treatment were done in conformity with common practice and were not motivated by the principle of deintensification. The patients' BP data in relation to antihypertensive treatment is shown in Table 4.

Table 4: Blood Pressure Relative to Antihypertensive Treatment

	Admission	Three Months Later
Supine BP, mmHg (Median)	123 / 74	121 / 69
No Patients on Anti-HT Medications	13 / 24	11 / 24
No of Anti-HT Drugs (Median)	3	1
Intensity of Anti-HT Treatment (Median)	1	0.5

Eleven out of 24 patients with a history of arterial hypertension had on admission normal BP without receiving antihypertensive medications. In one patient antihypertensives were discontinued: the BP remained within the normal range. In patients continuing to receive antihypertensive medications the dose and number of antihypertensive medications were reduced to get at goal BP (except one patient). Tapering antihypertensive treatment was unrelated to use of high dose opiate, sedative medications, inter current illness, dehydration, or end-stage cancer. Deintensification of antihypertensive treatment did not cause an overshoot of BP or any adverse event. A possible benefit of medication deintensification, as expected on theoretical grounds, could not be attested in the absence of a

comparator cohort group, though adverse effects of low BP might have been avoided.

g) Where Evidence is Scarce

Evidence-based medicine encourages the following of defined care pathways. Such evidence is evolving in patients with mild frailty but is not existing in patients with severe frailty and multimorbidity. Notably, comorbidities impact on benefits and harms of treatment (60-62). To enable physician decision making based on individualized expected outcomes, there is need to collect data focused at defined clinical categories, i.e., one or several chronic diseases in addition to advanced age and frailty (60-62). Observations from the bedside, enhanced and expanded, might contribute to a shift from empirical practice towards an evidence-balanced approach (61).

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