Ιδιαιτερότητες της υπέρτασης στους νεφροπαθείς

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Θεσσαλονίκη

Severity of hypertension travels with albuminuria, not eGFR

Hypertension Awareness, Treatment, and Control in Adults With CKD: Results From the Chronic Renal Insufficiency Cohort (CRIC) Study

	Overall No. (%)	Prevalence of Hypertension	Hypertension Control to < 140/90 mm Hg		Hypertension Control to < 130/80 mm Hg	
			Rate	Prevalence Ratio (95% confidence interval)	Rate	Prevalence Ratio (95% confidence interval)
eGFR (mL/min/1.73 m^2)						
<30	671 (19)	617 (92)	395 (64)	0.97 (0.89-1.04)	278 (45)	1.04 (0.89-1.21)
30-39	848 (23)	772 (91)	502 (65)	0.97 (0.90-1.05)	370 (48)	1.06 (0.91-1.23)
40-49	969 (27)	853 (88)	597 (70)	1.00 (0.93-1.08)	392 (46)	0.98 (0.86-1.14)
50-59	723 (20)	593 (82)	421 (71)	1.01 (0.94-1.10)	279 (47)	1.02 (0.88-1.19)
≥60	401 (11)	269 (67)	185 (69)	1.00 (reference)	118 (44)	1.00 (reference)

Multner P, et al. Am J Kidney Dis 2010;55:441-51

Correlates of Systolic Hypertension in Patients With Chronic Kidney Disease

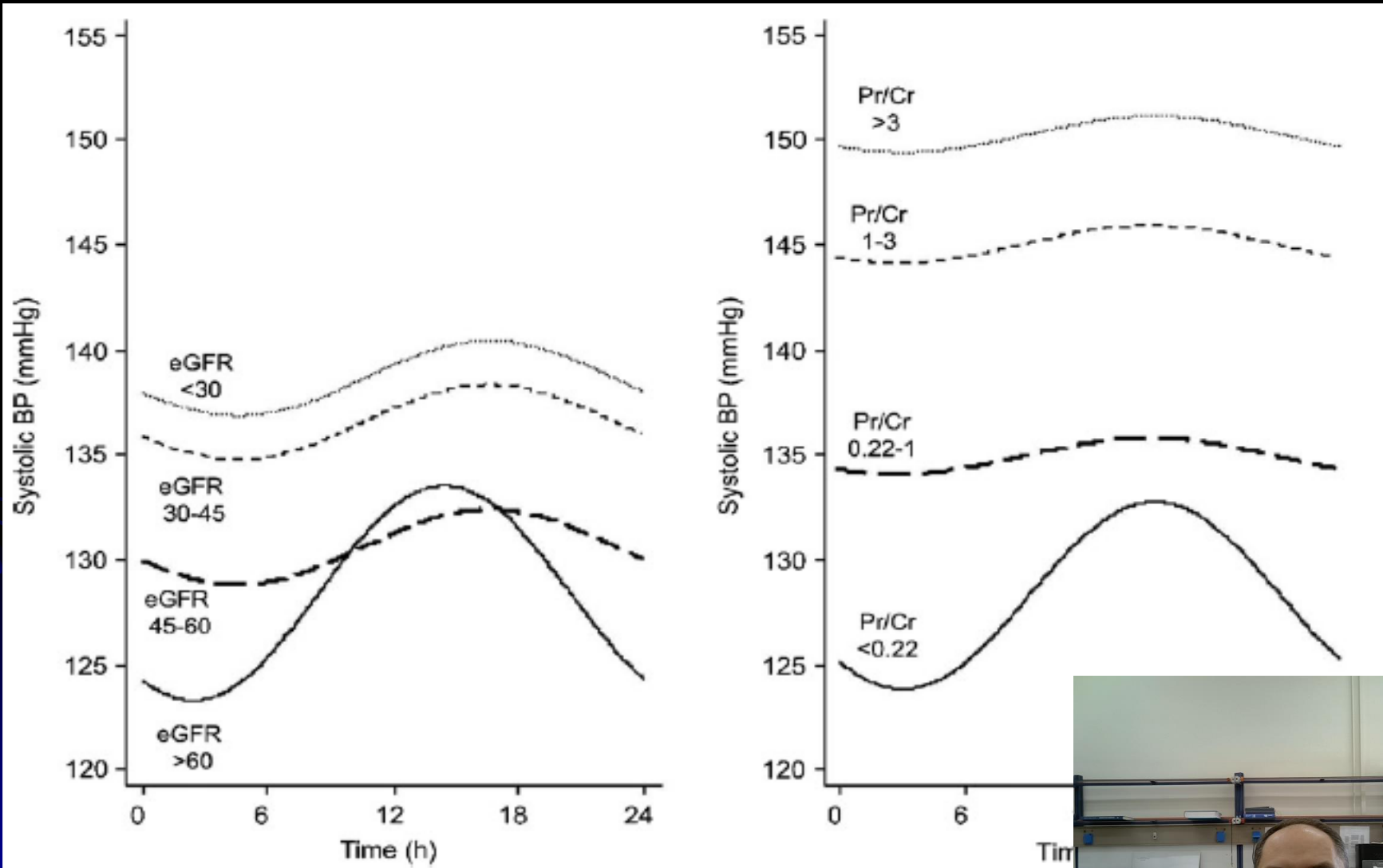| Risk Factors	Routine Clinic			Standardized Clinic			Home			24-Hour Ambulatory		
	Std β	r^2	P	Std β	r^2	P	Std β	r^2	P	Std β	r^2	P
Continuous variables												
Age	0.135	0.018	0.041	0.24	0.06	<0.0001	0.198	0.039	0.002			
Total cholesterol	0.16	0.026	0.015									
Log urine protein/creatinine	0.315	0.099	<0.0001	0.43	0.184	<0.0001	0.51	0.26	<0.0001	0.521	0.272	<0.0001
Albumin										−0.198	0.039	0.002
Hemoglobin				−0.254	0.064	<0.0001	−0.147	0.022	0.025	−0.230	0.053	<0.0001
Estimated GFR				−0.301	0.091	<0.0001	−0.286	0.082	<0.0001	−0.285	0.081	<0.0001
Dichotomous variables												
Race (white vs nonwhite)				−0.156	0.024	0.017	−0.138	0.019	0.036	−0.196	0.039	0.003
Etiology of renal disease (diabetes vs nondiabetes)				0.17	0.028	0.011	0.242	0.058	<0.0001	0.281	0.079	<0.0001
Alcohol use	−0.139	0.139	0.035	−0.133	0.018	0.043						
CAD	−0.167	0.028	0.011									
BP medication use	0.148	0.022	0.024	0.19	0.035	0.004	0.237	0.056				
No. of BP medications	0.153	0.023	0.020	0.28	0.276	<0.0001	0.338	0.114				

Correlates of Systolic Hypertension in Patients With Chronic Kidney Disease

Risk Factor	Routine Clinic	Standardized Clinic	Home	24-Hour Ambulatory
Age	0.172	0.212	0.145	
Total cholesterol	0.166			
Log urine protein/creatinine	0.272	0.369	0.451	0.461
Race (white vs nonwhite)		−0.120		−0.134
CAD	−0.213			
No. of BP medications	0.13	0.142	0.203	0.185
r^2	0.191	0.268	0.327	0.324
Adjusted r^2	0.173	0.255	0.318	
P	<0.0001	<0.0001	<0.000	

Agarwal R, et al. Hypertension 2005;46:514-520

GFR, proteinuria and circadian blood pressure

Agarwal R, et al. Nephrol Dial Transplant 2009;24:2400-06

Masked Uncontrolled Hypertension is very common in CKD

KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease

Chapter 1: Blood pressure measurement

> **Recommendation 1.1: We recommend standardized office BP measurement in preference to routine office BP measurement for the management of high BP in adults (1B).**

Practice Point 1.1: An oscillometric BP device may be preferable to a manual BP device for standardized office BP measurement; however, standardization emphasizes adequate preparations for BP measurement, not the type of equipment.
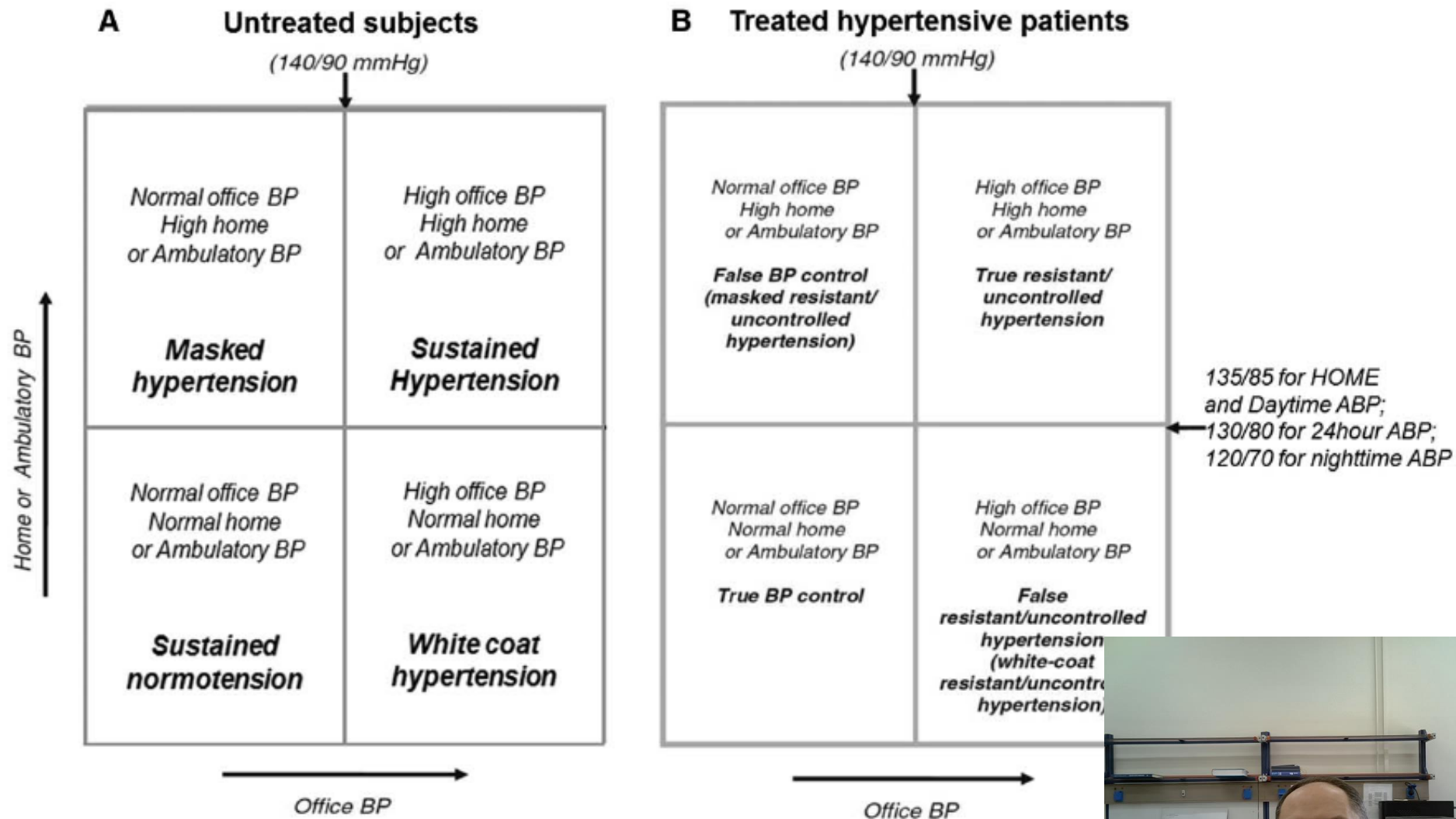
Practice Point 1.2: Automated office BP (AOBP), either attended or unattended, may be the preferred method of standardized office BP measurement.

Practice Point 1.3: Oscillometric devices can be used to measure BP among patients with atrial fibrillation.
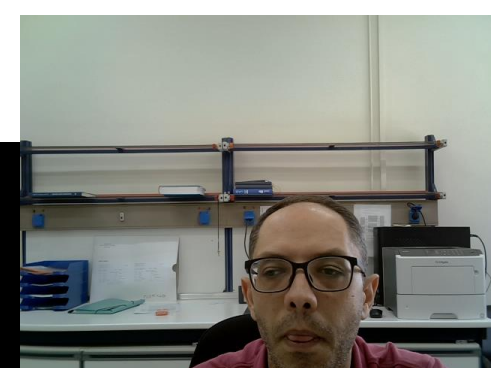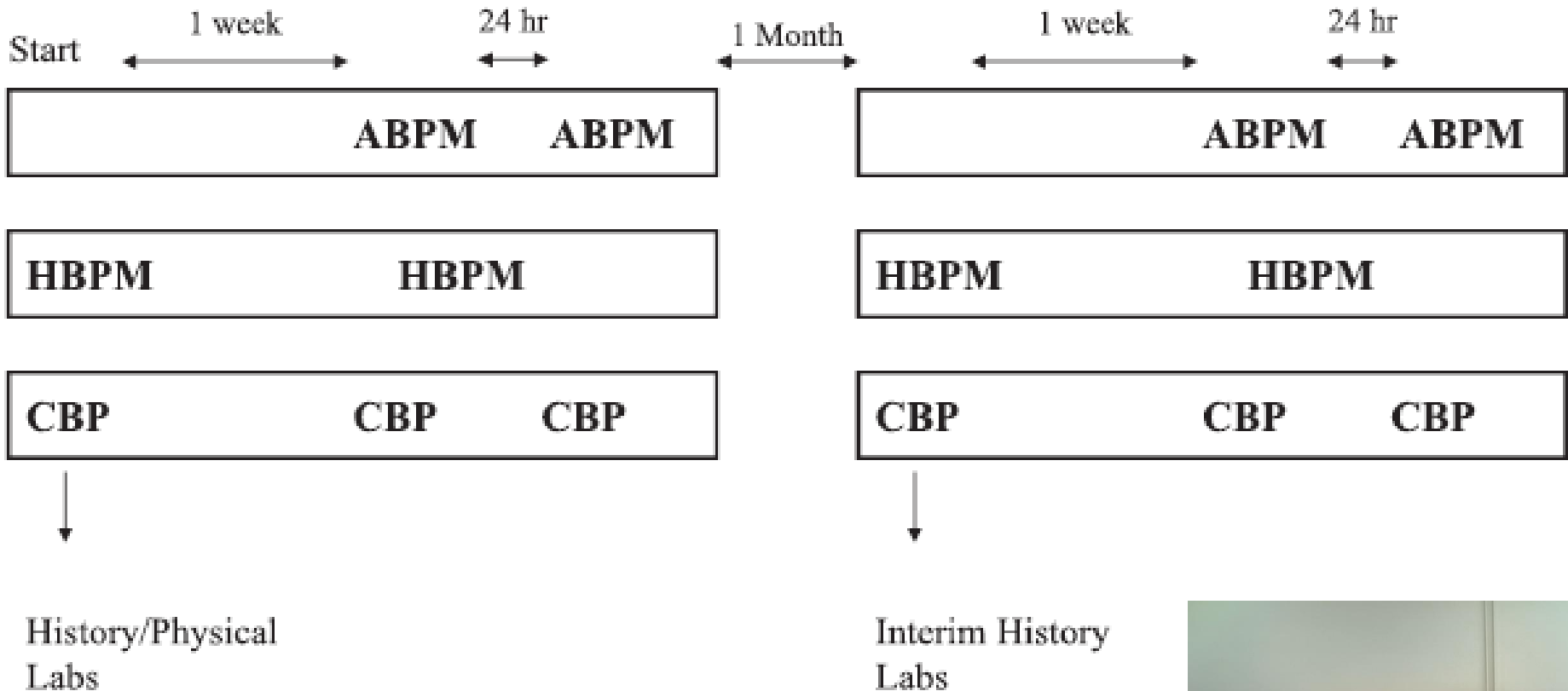
> **Recommendation 1.2: We suggest that out-of-office BP measurements with ambulatory BP monitoring (ABPM) or home BP monitoring (HBPM) be used to complement standa[...] for the management of high BP (2B).**

Cheung AK, et al. Kidney Int 2021; 99: S1-S87

Classification into BP phenotypes

A — Untreated subjects (140/90 mmHg)

Normal office BP, High home or Ambulatory BP — **Masked hypertension**	High office BP, High home or Ambulatory BP — **Sustained Hypertension**
Normal office BP, Normal home or Ambulatory BP — **Sustained normotension**	High office BP, Normal home or Ambulatory BP — **White coat hypertension**

Home or Ambulatory BP / Office BP

B — Treated hypertensive patients (140/90 mmHg)

Normal office BP, High home or Ambulatory BP — **False BP control (masked resistant/uncontrolled hypertension)**	High office BP, High home or Ambulatory BP — **True resistant/uncontrolled hypertension**
Normal office BP, Normal home or Ambulatory BP — **True BP control**	High office BP, Normal home or Ambulatory BP — **False resistant/uncontrolled hypertension (white-coat resistant/uncontrolled hypertension)**

135/85 for HOME and Daytime ABP; 130/80 for 24hour ABP; 120/70 for nighttime ABP

Parati G, et al. Hypertension 2016; 67(6):1093-101.

Masked Uncontrolled Hypertension in CKD

Agarwal R, et al. J Am Soc Nephrol 2016; 27: 924-932

Masked Uncontrolled Hypertension in CKD

a) Prevalence of MUCH in CKD

	Baseline visit				Repeat visit at 4 weeks			
	CH (n)	UCH (n)	MUCH (%)	95% CI	CH (n)	UCH (n)	MUCH (%)	95% CI
Daytime ABPM	192	70	26.7	21.3–32.1%	177	69	28.0	22.4–33.7%
24-Hour ABPM	176	86	32.8	27.1–38.5%	154	92	37.4	31.3–43.5%
Daytime and nighttime ABPM	115	147	56.1	50.1–62.2%	106	140	56.9	50.7–63.1%
Home BP	140	122	46.6	40.5–52.6%	132	114	46.3	40.1–52.6%

b) Prevalence of MUCH according to the levels of clinic SBP

Clinic systolic BP (mmHg)	Baseline visit					Return visit at 4 weeks				
	CH (n)	UCH (n)	MUCH (%)	OR (95% CI)	aOR	CH (n)	UCH (n)	MUCH (%)	OR	aOR
<110	66	1	1.5	1	1	62	3	4.6	1	1
110–119	69	14	16.9	13.4 (1.7–104.7)	9.1 (1.1–74.9)	53	11	17.2		
120–129	39	20	33.9	33.8 (4.4–262.1)	21.2 (2.6–172.1)	43	29	40.3		
130–139	18	35	66.0	128.3 (16.4–1001.8)	90.3 (11.1–734.3)	19	26	57.8		

Agarwal R, et al. J Am Soc Nephrol 2016; 27: 924-932

Masked Uncontrolled Hypertension in CKD

c) Reproducibility of MUCH in CKD

	Concordance statistics			
	Agreement	κ	95% CI κ	P level
Daytime ABPM	78.4%	0.441	0.305–0.577	<0.001
24-Hour ABPM	76.5%	0.474	0.339–0.609	<0.001
Daytime and nighttime ABPM	75.5%	0.509	0.372–0.645	<0.001
Home BP	62.8%	0.249	0.112–	

Agarwal R, et al. J Am Soc Nephrol 2016; 27: 924-932
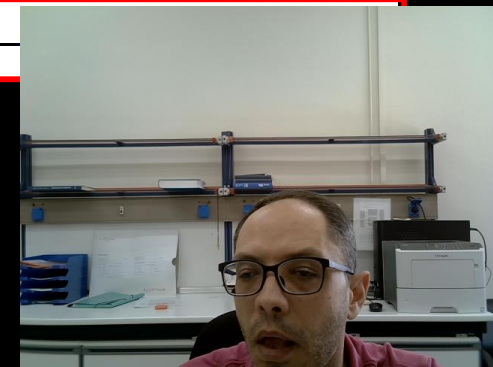
Masked Uncontrolled Hypertension in CKD

d) HBP vs. Clinic BP monitoring for diagnosing MUCH in CKD

Agarwal R, et al. J Am Soc Nephrol 2016; 27: 924-932
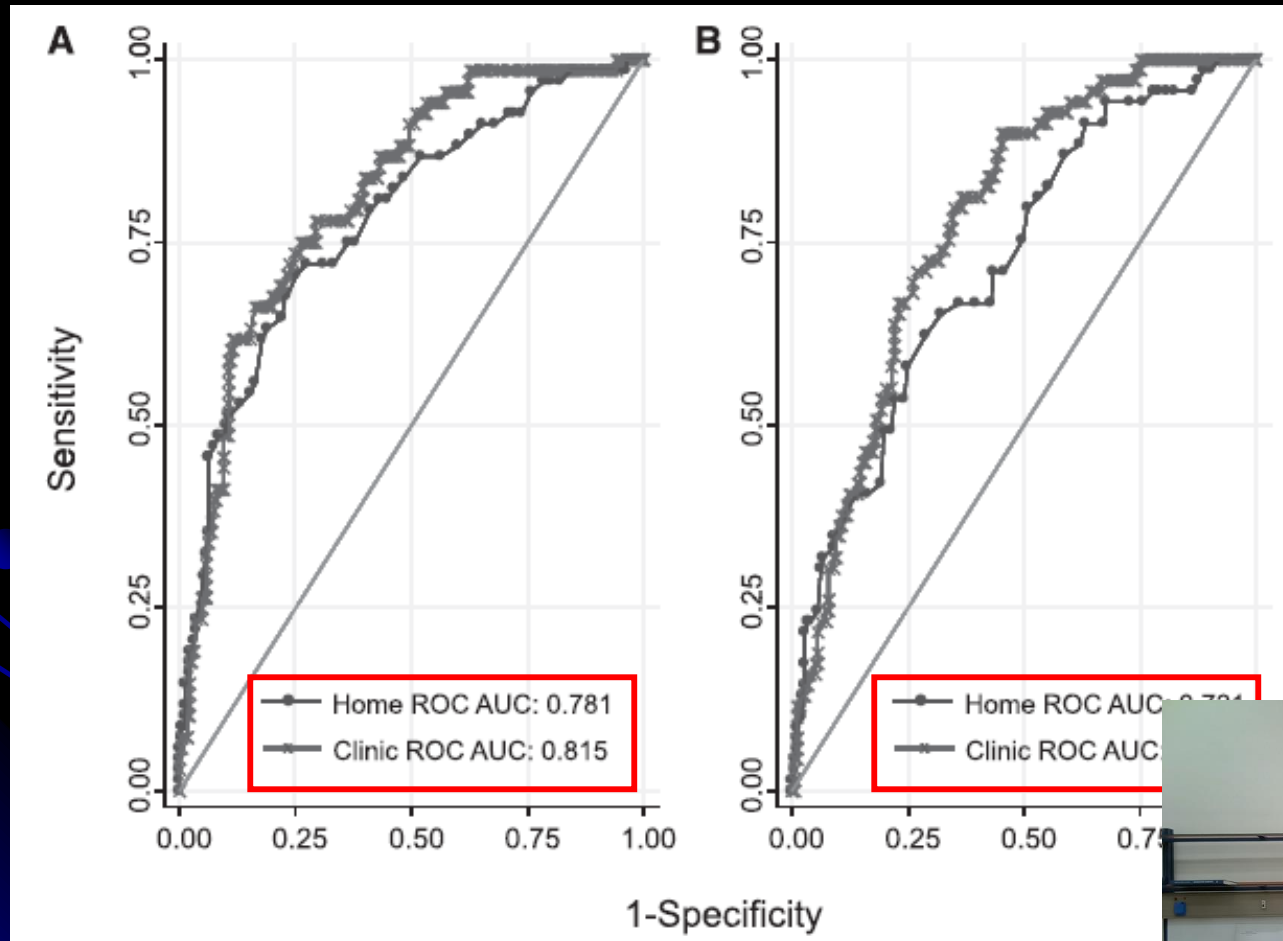
Prognostic Significance of Ambulatory BP Monitoring in CKD: A Report from the Chronic Renal Insufficiency Cohort (CRIC) Study

e) Prognostic significance of MUCH in CKD
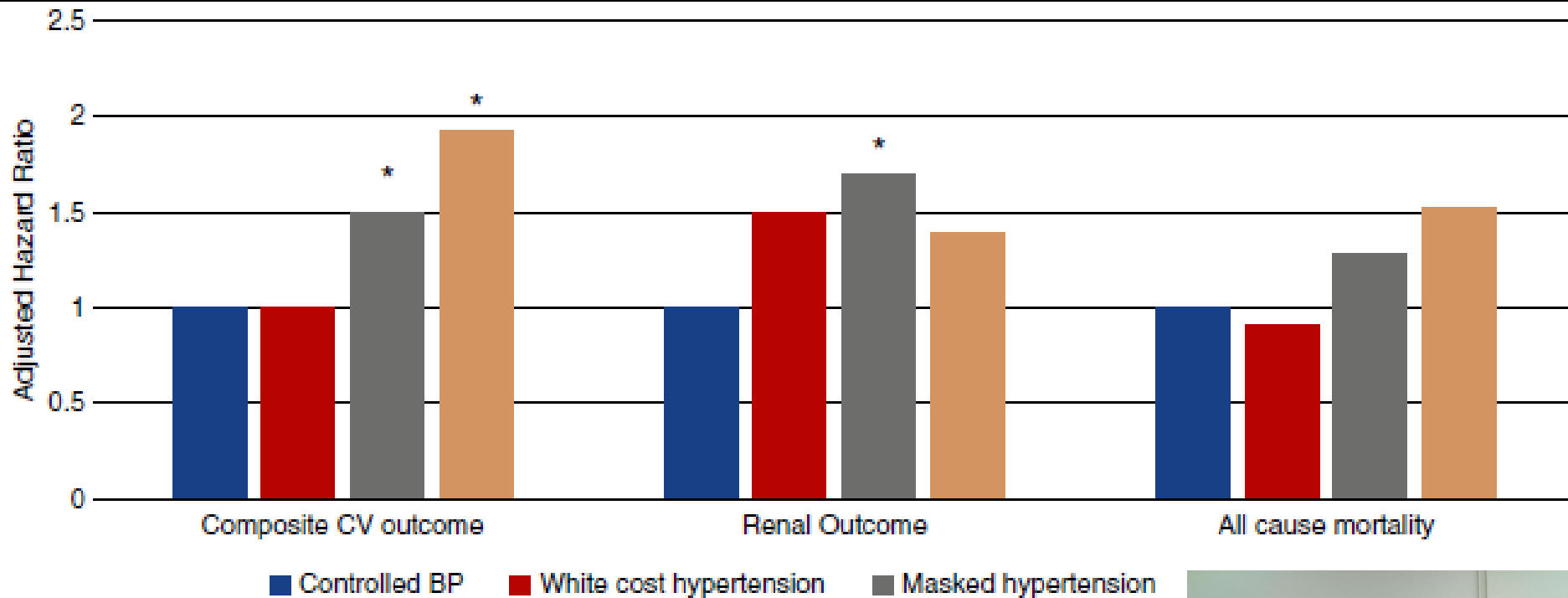
*P<0.05, compared to patients with controlled Blood Pressure

Rahman M, et al. J Am Soc Nephrol 2020; 31: 2609-21.

Hypertension in CKD is very often resistant to antihypertensive therapy

Definitions

Hypertensive phenotype	Abbreviation	Definition
Refractory hypertension	RfH	BP ≥140/90 while prescribed ≥5 antihypertension medication classes, including a diuretic
Treatment-resistant hypertension	TRH	BP ≥140/90 while prescribed 3 or 4 antihypertension medication classes, including a diuretic
		OR
		BP <140/90 while prescribed ≥4 antihypertension medication classes, including a diuretic
Responsive hypertension	Non-TRH/RfH	BP ≥140/90 while prescribed 1 or 2 antihypertension medication classes, including a diuretic
		OR
		BP ≥140/90 while prescribed any antihypertension medication, not including a diuretic
		OR
		BP ≥140/90 while not prescribed antihypertension medication
		OR
		BP <140/90 while prescribed 1, 2, or 3 a classes, including a diuretic
		OR
		BP <140/90 while prescribed any antihyp including a diuretic

Buhnerkempe M, et al. Hypertension 2021; 77: 72-81

Global prevalence of resistant hypertension: a meta-analysis of data from 3.2 million patients

True resistant hypertension

Study	Events	Total	Prevalence, %	95%-CI	Weight
Barochiner, 2012	21	289		7.27 [4.55; 10.89]	7.8%
Brambilla, 2013	255	1312		19.44 [17.33; 21.68]	8.7%
Brown, 2001	85	334		25.45 [20.86; 30.48]	7.9%
Chio, 2016	134	1230		10.89 [9.21; 12.77]	8.6%
De La Sierra, 2011	5184	68045		7.62 [7.42; 7.82]	8.9%
De Nicola, 2011	79	550		14.36 [11.54; 17.58]	8.3%
Gijon−Conde, 2015	25	720		3.47 [2.26; 5.08]	8.4%
Mezzetti, 1997	3	250		1.20 [0.25; 3.47]	7.7%
Naseem, 2017	62	515		12.04 [9.36; 15.17]	8.3%
Pierdomenico, 2005	130	1715		7.58 [6.37; 8.94]	8.7%
Salvetti, 2011	45	478		9.41 [6.95; 12.39]	8.2%
Yaméogo, 2014	101	692		14.60 [12.05; 17.45]	
Overall prevalence		76130		10.25 [7.65; 13.19]	

Heterogeneity: $I^2 = 97.1\%$ [96.1%; 97.9%], $\tau^2 = 0.0060$, $p < 0.0001$

5 10 15 20 25 30

Noubiap JJ, et al. Heart 2019;105: 98-105.

Prevalence and Prognostic Role of Resistant Hypertension in Chronic Kidney Disease Patients

	Control (n = 118)	Pseudoresistance (n = 31)	Sustained Hypertension (n = 187)	True Resistance (n = 100)
Office systolic BP	139 ± 17	148 ± 14	146 ± 18	154 ± 20
Office diastolic BP	79 ± 10	82 ± 8	84 ± 12	82 ± 12
Office systolic BP ≥130 mm Hg	80 (67.8)	28 (90.3)	153 (81.8)	94 (94.0)
Office diastolic BP ≥80 mm Hg	63 (53.4)	20 (64.5)	133 (71.1)	68 (68.0)
Daytime systolic BP	116 ± 9	115 ± 8	138 ± 13	144 ± 16
Daytime diastolic BP	68 ± 7	65 ± 6	81 ± 10	76 ± 10
Nighttime systolic BP	106 ± 9	106 ± 9	127 ± 17	138 ± 19
Nighttime diastolic BP	60 ± 6	57 ± 7	70 ± 9	70 ± 10
Nondippers	75 (63.6)	19 (61.3)	102 (54.5)	74 (74.0)
BP-lowering drugs	1.9 ± 1.0	3.8 ± 0.9	1.8 ± 1.2	4.2 ± 1.1
0 drug	9	—	32	—
1 drug	40	—		
2 drugs	45	—		
3 drugs	22	19		
>3 drugs	2	12		

De Nicola L, et al. J Am Coll Cardiol 61(24):2461-2467.

Prevalence and Prognostic Role of Resistant Hypertension in Chronic Kidney Disease Patients

Table 3	Multivariable Cox Models for CV and Renal Outcomes	
	CV Outcome	**Renal Outcome**
Age (1-yr)	1.06 (1.04–1.08)*	1.00 (0.99–1.02)
Male	2.32 (1.49–3.61)*	1.46 (1.05–2.05)*
BMI (1-kg/m^2)	0.98 (0.94–1.02)	0.99 (0.96–1.02)
Diabetes (yes vs. no)	1.32 (0.87–2.01)	0.89 (0.62–1.26)
History of CV events (yes vs. no)	2.04 (1.37–3.03)*	1.11 (0.78–1.59)
Log-proteinuria	0.99 (0.72–1.36)	1.35 (1.04–1.75)*
GFR (ml/min/1.73 m^2)	0.98 (0.97–0.99)*	0.93 (0.92–0.95)*
Groups		
Control	Reference	Reference
Pseudoresistance	1.24 (0.55–2.78)	1.18 (0
Sustained hypertension	1.11 (0.67–1.84)	2.14 (1
True resistance	1.98 (1.14–3.43)*	2.66 (1
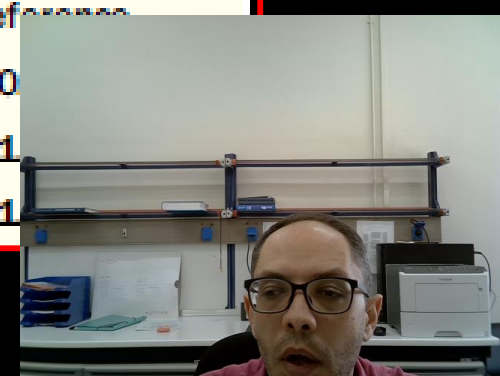
De Nicola L, et al. J Am Coll Cardiol 61(24):2461-2467.

Adverse Health Outcomes Associated With Refractory and Treatment-Resistant Hypertension in the Chronic Renal Insufficiency Cohort

Characteristic	Hypertensive phenotype			P value	
	Non-TRH/RfH (n=2006)	TRH (n=1005)	RfH (n=136)	Non-TRH/RfH vs TRH	TRH vs RfH
Age, y, mean (SD)	57.9 (11.0)	61.0 (9.2)	60.9 (8.9)	<0.01	0.90
Women, n (%)	891 (44)	438 (44)	56 (41)	0.69	0.66
Race, n (%)				<0.01	0.04
Non-Hispanic White	898 (45)	296 (29)	28 (21)		
Non-Hispanic Black	788 (39)	531 (53)	89 (65)		
Hispanic	251 (13)	136 (14)	16 (12)		
Other	69 (3)	42 (4)	3 (2)		
Education, n (%)				<0.01	0.67
Less than high school	392 (20)	264 (26)	38 (28)		
High school graduate	374 (19)	212 (21)	31 (23)		
Some college	585 (29)	313 (31)	44 (32)		
College graduate and above	655 (33)	216 (21)	23 (17)		
Diastolic BP, mm Hg, mean (SD)	72.4 (12.4)	70.6 (13.6)	78.8 (16.3)		
Systolic BP, mm Hg, mean (SD)	126.6 (19.7)	135.4 (23.3)	158.7 (14.8)		
eGFR, mL/min per 1.73 m², median (IQR)	44.7 (34.0–55.4)	36.9 (28.4–47.4)	34.9 (26.8–49.2)		

Buhnerkempe M, et al. Hypertension 2021; 77: 72-81

Adverse Health Outcomes Associated With Refractory and Treatment-Resistant Hypertension in the Chronic Renal Insufficiency Cohort

Outcome	Non-TRH/RfH	TRH	RfH
CVD composite (stroke/MI/CHF)			
Events per 1000 person years	28.8	65.1	122.1
HR (95% CI)– years 0–3	0.69 (0.55–0.85)	Reference†	1.25 (0.91–1.73)
HR (95% CI)– years 3–6	0.59 (0.46–0.77)	Reference	1.50 (0.97–2.32)
HR (95% CI)– years 6–10	1.06 (0.73–1.56)	Reference	2.72 (1.47–5.01)
Renal composite (50% eGFR decline/ESRD)			
Events per 1000 person years	52.8	95.8	190.6
HR (95% CI)– years 0–10	0.81 (0.71–0.93)	Reference	1.73 (1.

Buhnerkempe M, et al. Hypertension 2021; 77: 72-81
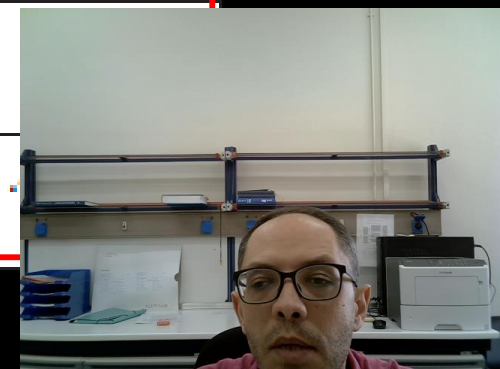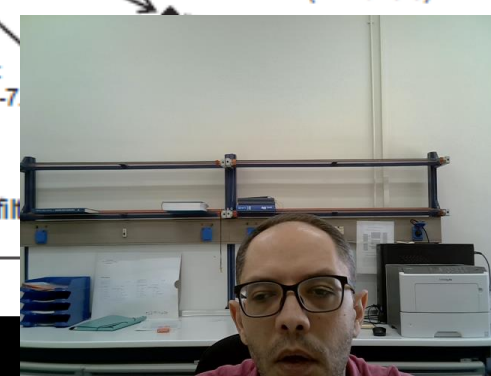
Volume-mediated Hypertension in ESKD

Dry-Weight Reduction in Hypertensive Hemodialysis Patients (DRIP)
A Randomized, Controlled Trial

Agarwal R, et al. Hypertension 2009;53(3):500-7.

Dry-Weight Reduction in Hypertensive Hemodialysis Patients (DRIP)
A Randomized, Controlled Trial

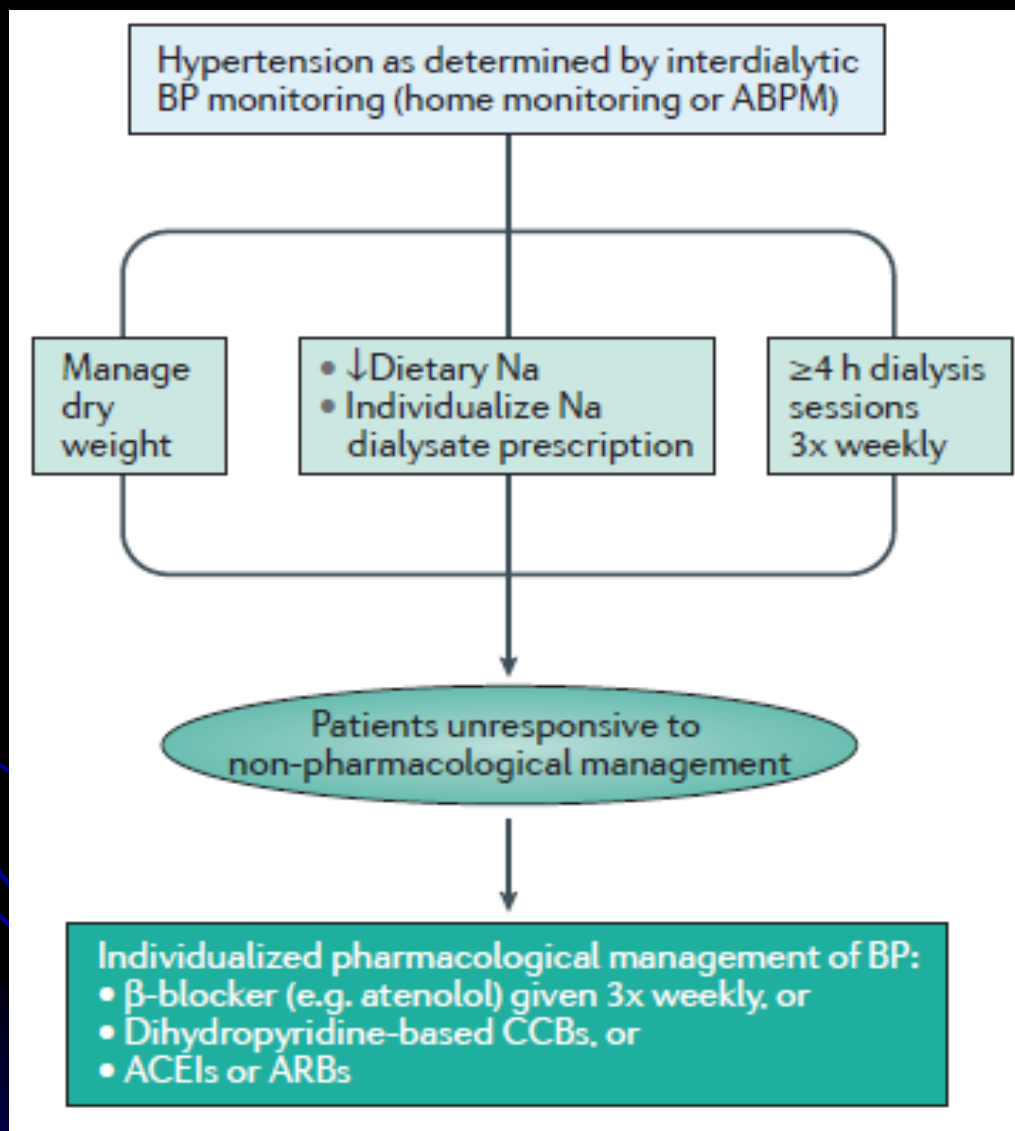*Agarwal R, et al. Hypertension 2009;53(3):500-7.*
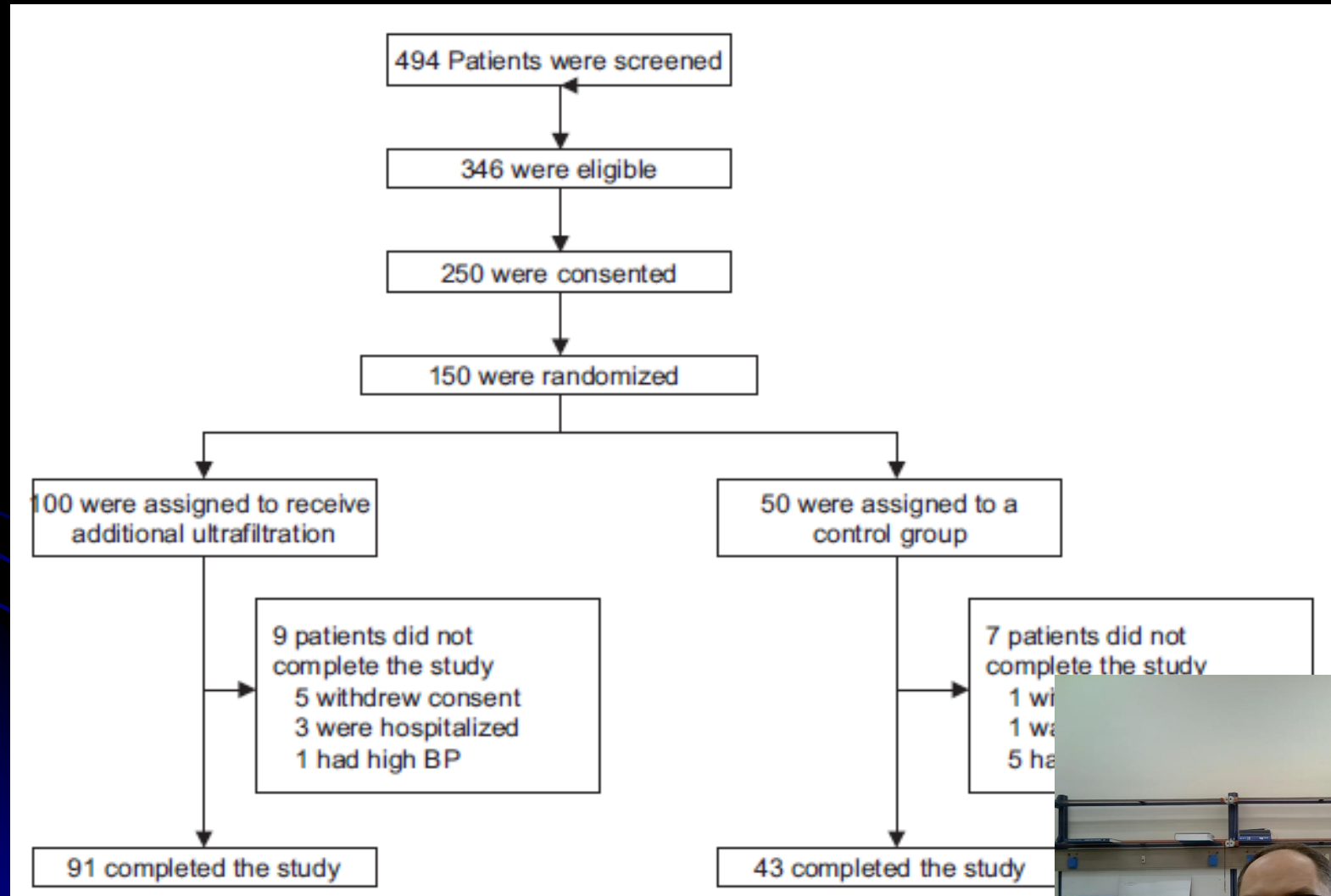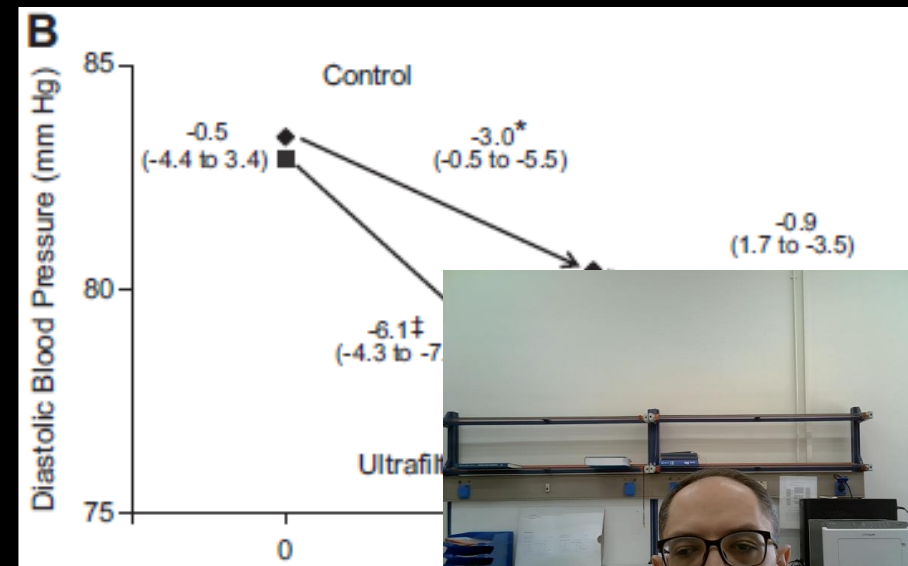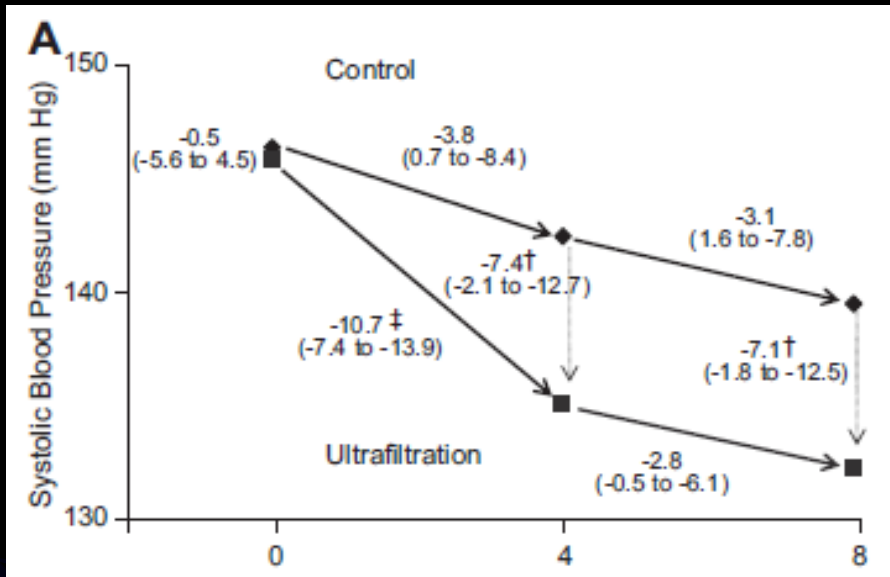
Probing Dry-Weight Improves Left Ventricular Mass Index

Echocardiographic volume parameter	Intervention group	Baseline				Week 4 change from baseline				Week 8 change from baseline			
		n	mean	95% CI	p	n	mean	95% CI	p	n	mean	95% CI	p
LVMI, g/m^2	control	38	136.3	125.1, 147.5		31	3.5	−3.3, 10.3	>0.2	31	0.3	−8.1, 8.8	>0.2
	UF	72	138.7	130.6, 146.8		57	−7.4	−12.5, −2.3	0.005*	63	−6.3	−12.5, −0.1	0.045*
	UF – control		2.5	−11.4, 16.3	>0.2		−10.9	−19.4, −2.4	0.012*		−6.6	−17.1, 3.8	>0.2
IVSd, cm	control	38	1.31	1.24, 1.37		31	0.02	−0.01, 0.05	>0.2	31	0	−0.04, 0.03	>0.2
	UF	72	1.32	1.27, 1.37		57	0.01	−0.01, 0.03	>0.2	63	0.01	−0.02, 0.04	>0.2
	UF – control		0.01	−0.06, 0.09	>0.2		−0.01	−0.05, 0.02	>0.2		0.01	−0.03, 0.06	>0.2
LVId, cm	control	38	5.05	4.84, 5.26		31	−0.01	−0.16, 0.14	>0.2	31	−0.06	−0.22, 0.11	>0.2
	UF	72	4.98	4.83, 5.13		57	−0.22	−0.33, −0.11	<0.001*	63	−0.19	−0.31, −0.07	0.002*
	UF – control		−0.07	−0.33, 0.19	>0.2		−0.21	−0.40, −0.02	0.030*		−0.13	−0.34, 0.07	>0.2
LVPWd, cm	control	38	1.25	1.20, 1.31		31	0.04	0.00, 0.07	0.025*				
	UF	72	1.29	1.25, 1.33		57	0.01	−0.01, 0.03	>0.2				
	UF – control		0.04	−0.03, 0.10	>0.2		−0.03	−0.07, 0.01	0.19				
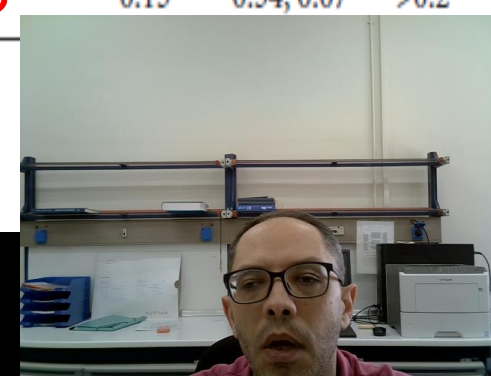
Algorithm for the diagnosis and management of hypertension in HD

Georgianos PI & Agarwal R. Nat Rev Nephrol 2016;12(10):636-47.