American Heart Association.
Hypertension

Chat Discussions
Thursday, September 10, 2020

Welcome Remarks and Keynote Lecture

name	message
Matthew Sparks	Excited for the sessions.
Mitchell Elkind	Good morning and welcome to Hypertension Sessions!
Mary Haynes	Good Morning
Curt Sigmund	Welcome all! Glad you all found your way to the virtual room!
Andrew South	Looking forward to an excellent virtual conference.
Stephanie Watts	Curt, Good morning to you from East Lansing!
Mary Macleod	Hello from Scotland
Mahmoud Abdelbary	I am so excited.
Jan Basile	Curt, can not thank you and everyone else for their work in getting us to this point! Bravo!
Yagna Jarajapu	Hello from NDSU, Fargo ND.
Daichi Shimbo	Welcome everyone!
Yagna Jarajapu	Good morning!
Junie Warrington	Hello everyone! Glad to be able to join virtually!
David Pollock	Hi all, gladto be here. Only took me 10 minutes and about 100 clicks to find this session.
Kristi Reynolds	Good Morning from Los Angeles!
Mary Haynes	Future has met us head on. Looking forward to information and technology combination.
Curt Sigmund	Make sure you push the arrow on the screen.
Augusto Montezano	Hi all, a huge hello from the UK! Excited to be here!
Dulce Casarini	Dear Curt, thank you and everyone else for their work for this meeting
Aaron Trask	Good morning from Columbus!
Annet Kirabo	Too many clicks. I wonder if this can be simplified a bit
Nirupama Ramkumar	Good morning from Salt Lake City !
Rhian Touyz	Looking forward to a great meeting and a new experience. Hi and best to all
Mark Santillan	Good morning from Iowa!
Stephen Juraschek	Congratulations to award winners!
Emily Andaya	Good morning from Indiana!
Anastasia Mihailidou	Greetings all from Sydney near midnight
Stephanie Watts	Yay Bob and Anna! Fantastic!

PaulIvan Torres	Hello everyone! from the Philippines
Jorge Galperin	good morning from Buenos Aires
Mitchell Elkind	Congratulations to all award winners!
William Cushman	Congratulations to all awardees! Well deserved!
Gregory Fink	Excellent awardees. Congrats to all.
Camilla Wenceslau	Good morning!
John Imig	Good morning everyone!
HanNaung Tun	Good Morning everyone , from Henry Han @HanCardiomd
Eric BelinDeChantemele	Morning everyone from GA
Anne Kwitek	Good morning from Wisconsin.
Curt Sigmund	Hello from Milwaukee!
Hana Itani	Hello from Beirut, Lebanon!
Maria SequeiraLopez	Hello from Cville, VA!
Wendy Bollag	Hello from Augusta
Junie Warrington	So good to see all the familiar names! Hello from Mississippi!
Styliani Goulopoulou	Good morning from Fort Worth, Texas!
Karen Griffin	Hello from Chicago!
Curt Sigmund	I want to thank all members of the Program Committee particularly Dr. Daichi Shimbo and his team for coordinating the clinical program.
Sebastiao FerreiraFilho	Hello from Brazil!
Simone BrixiusAnderko	Good morning from Ann Arbor!
Mahboob Rahman	Greetings from Cleveland
Mahboob Rahman	Greetings from Cleveland
Jami Burkhardt	Good morning from Minnesota!
Owen Richfield	Hello from New Orleans! Sad to not be able to see y'all here in person, but glad to connect virtually!
William Cushman	Good morning from Memphis!
Barry Davis	Greetings from Houston
cheryl curtis	hello from ottawa!! Wish we were in New Orleans again
Lois Katz	Good morning from rainy New York City
Jeffrey Bates	Howdy from Houston!
Marian Manalo	Good evening from the Philippines
Tariq Qureshi	Good morning from Toronto
Dave Dixon	Good morning from Richmond, Virginia!
Justin VanBeusecum	Good morning from Nashville, TN!
Dewan Majid	Hellow everybody
Swapnil Hiremath	good morning from Ottawa! Exciting for all the sessions and debates
Styliani Goulopoulou	It is great that colleagues from all over the world can join!

Eman Gohar	Good morning everyone!
Uche Iheme	Good day from Cleveland, OH
Xiaoqing Pan	Greetings from China!
Marc Cook	Morning from Greensboro, NC
Curt Sigmund	Thank you Dr. Elkind.
Michael Ernst	Hello from Iowa City, IA
Alexander Staruschenko	Thank you Dr. Elkind! Looking forward to great HTN/KCVD (ASH) meeting!
Lorena Citterio	Greeting from Milano, Italy!
PaulIvan Torres	Greetings from Las Pinas Philippines!
Mitchell Elkind	Looking forward to an exciting and educational meeting!
Jordana Cohen	Good morning, from Philly! Great to see so many familiar names
Curt Sigmund	I want to thank my colleagues in the KCVD particularly Vivek Bhalla and Alexander Staruschenko for their efforts on behalf of the conference.
Xiaohan Lu	Greetings from Durham, NC.
Jane Reckelhoff	Hey y'all from Jackson, MS!
Catherine LlorensCortes	Hello from Paris
Eric Lazartigues	Good morning from New Orleans! (where the meeting was supposed to be)
ArnoldBenjamin Mina	:-)
Sabrina Scroggins	Good morning!
Mitchell Elkind	Thanks to all the organizers of the meeting, especially Drs. Sigmund, Bhalla and Shimbo!
David Pollock	at Birmingham
Daichi Shimbo	Thank you Dr. Jordana Cohen & Dr. John Bisognano, and Dr. Ian Kronish & Dr. Mike Rakotz on being co-chairs of the clinical practice and clinical science track, and the primary care track respectively.
Maria SequeiraLopez	���� to all the awardees!!!!
Maria SequeiraLopez	Those were clapping hands!!!!
Joey Granger	Congrats to all awardees!!
Frank Spradley	Hello All from Jackson, MS. Thanks to the organizers that worked to make this meeting still possible.
Liliya Yamaleyeva	Good morning from North Carolina
Curt Sigmund	Congratulations to Dr. Ute Scholl on her selection as our Keynote Lecturer. Thank you Ute!
Roshni Patel	Good morning from Maryland!
Curt Sigmund	Please restrict chat with questions for the speaker. Send your questions to Dr. Scholl through chat for her to answer in real time.

Mitchell Elkind	Thank you Dr. Griffin for your leadership of the Council. Have a great meeting.
Vim Samonte	Good morning from Philippines!
Analia Loria	Good Morning from Lexington, KY! Looking forward for a great virtual meeting. Thanks for all the efforts to make this happen.
Sumit Monu	Good morning from Henry Ford Hospital, Detroit
Karen Griffin	Thank you Dr. Elkind and Best of Luck as our Commander in Chief!
Frederique Yiannikouris	Hello from Lexington, KY!
Owen Richfield	Hi Sumit!
Sumit Monu	Hi Owen!!
Emily Andaya	Good morning to those from the Philippines from Indianapolis, Indiana
Leah Polidario	Greetings! from Palo, Leyte Philippines..
Marian Manalo	Good evening here in the Philippines
David Pollock	Why is eplerenone not available in Europe and other countries?
Swapnil Hiremath	Dr Scholl: any comments on the recent paper suggesting 24 hour urinary aldosterone is more sensitive compared to ARR for diagnosis of PA? https://pubmed.ncbi.nlm.nih.gov/32449886/
Ute Scholl	It is available, but only approved for the therapy of heart failure, so it is used off label for primary aldosteronism.
David Pollock	I see, thanks.
Ute Scholl	Interesting study using 24 h u aldosterone - this will most likely recognize cases that are quite different from those diagnosed using the traditional criteria. Likely milder cases will be recognized.
David Pollock	What factors are involved in choosing spironolactone versus eplerenone?
David Harrison	I almost always use eplerenone.
Ute Scholl	In Europe, we usually try Spironolactone first. If side effects occur, we change to Eplerenone (off label). Other factors to consider are cost (higher cost for Eplerenone) and age (Eplerenone preferred in children / adolescents because of Spironolactone side effects)
Ute Scholl	Outside Europe, Eplerenone as first choice would make more sense
William Cushman	I know eplerenone is more expensive, but I thought it might be less potent, but I don't know any data.
Ute Scholl	About twice the dose of Spironolactone is required
Uche Iheme	Does Eplerernone have comparative CV benefits (relative to Spironolactone) in patients with co-morbid HFrEF?
Nora Franceschini	Is there a way to screen for these somatic mutations without having tumor tissue?

Alexander Staruschenko	Does Kcnj5 forms heteromeric channel only with Kcnj3 or it can interact and form functional channel with other Kir channels?
Ute Scholl	Eplerenone does have CV benefits in HFrEF in general, but I am not aware of studies in primary aldosteronism specifically
Camilla Wenceslau	what about NCX?
Ute Scholl	At this point, it is not possible to screen for somatic mutations without having tumor tissue
David Harrison	Eplerenone was studied in the Emphasis HF trial and was very effective. Not aware of studies comparing the two head to head.
Ute Scholl	KCNJ5 can also form homotetramers
Ute Scholl	Sorry, what specifically was the question about NCX?
Spencer Cushen	Sorry if this sounds uninformed, but do the tumors shed tissue into the renal vein blood that could be collected during RVS? Or is this impractical
Camilla Wenceslau	does it chance in the presence of NaKATPase mutation? or in tumor?
Nora Franceschini	I wonder if one can capture some of the cells and/or through circulating exosomes for diagnosis
Ute Scholl	Interesting thought! These are benign tumors, so any DNA shed into the adrenal vein would be scarce. We have so far not been able to detect cell-free DNA from tumors.
Spencer Cushen	Thank you Dr. Scholl
Thu Le	When would you recommend adrenal biopsy to screen for mutations?
Ute Scholl	NCX might be able to counteract to some extent the elevated intracellular calcium levels caused by mutations, but I am not aware of any data examining this directly - would have to check the literature.
Camilla Wenceslau	Thank you Dr. Scholl
Ute Scholl	I would not recommend adrenal biopsy to screen for mutations at all. At this point, there is no clinical indication for mutation screening in APAs.
Ute Scholl	If APA is confirmed clinically, then the recommendation would be to perform adrenalectomy, regardless of the mutation status.
Thu Le	What about in the case of bilateral adrenal hyperplasia?
Fernando Elijovich	Is angiotensin II mutagenic in aldosterone producing cells? In other words, could adrenal hyperplasia be tertiary rather than primary hyperaldosteronism?
Ute Scholl	In those patients, the clusters are tiny. So those are almost impossible to catch by biopsy. The recommendation would be to treat with MR antagonists.

Henry Chan	In some cases of PA are normokalemic, when will you suspect patients having PA?
James Luther	Glad that APCCs are being highlighted- this is one recent advance that has not been widely appreciated yet.
Ute Scholl	Tertiary aldosteronism: very interesting thought. ATII, when chronically elevated, does cause glomerulosa hyperplasia. But unlike tertiary hyperparathyroidism, tertiary hyperaldosteronism isn't a known clinical entity.
Ute Scholl	The majority of PA patients (in particular those with bilateral hyperplasia) are normokalemic, so patients with severe / resistant hypertension should be screened regardless of serum potasssium levels.
Henry Chan	Thank you, Dr. Scholl
Andrew South	Dr. Scholl, does your recommended screening approach differ in children compared to adults?
Ute Scholl	Because primary aldosteronism is so rare in childhood, there are no clear guidelines (as far as I know, but I do not see pediatric patients). I would recommend using the ARR as a screening parameter.
Andrew South	Thank you, Dr. Scholl. And wonderful talk.
Ute Scholl	Because incidentalomas are very rare in childhood, the presence of an adrenal adenoma in childhood combined with primary aldosteronism I think would be a strong indication of aldosterone-producing adenoma
Ute Scholl	So likely no need for AVS in those cases
HanNaung Tun	Fantastic lecture on genetic of primary aldosteronisms . What about the role of genetic panel testing and its cost effective in clinical practice ?
Ute Scholl	Thank you! Panel testing for germline mutations in my view makes sense when familial hyperaldosteronism is suspected (early onset and/or positive family history). It is not suitable for GRA, however, which is the most common form of familial hyperaldosteronism and should be tested first.
Ute Scholl	Panel testing for somatic mutations at this point is only used in research
John Floras	Dr. Scholl, can you propose a mechanism to explain why bilateral adrenal hyperplasia is so often present in hypertensive men with obstructive sleep apnea?
Curt Sigmund	Thank you Dr. Scholl for your fantastic talk. Virtual applause!!!!!
Daichi Shimbo	Thank you, Dr. Scholl. GREAT talk.
Ute Scholl	I suppose volume overload contributes to sleep apnea
Joshua Samuels	Excellent. thanks

Ute Scholl	Thank you!
Bharathi Upadhya	great talk
Dulce Casarini	Thank you execelent talk
Anne Kwitek	Great talk Dr Scholl! Thank you
Dave Dixon	Terrific talk! Thank you
Styliani Goulopoulou	Excellent talk!
Christine Klemens	Great talk, thank you!
Marwah Abdalla	Fantastic talk!
Atossa Niakan	Thank you so much for great talk
Matthew Alexander	Great talk. Thank you!
Justin Grobe	Thank you!
Simone BrixiusAnderko	Thank you for this great talk!
Anna Oliveras	Great !!!
Norman Jurado	That was excellent. Thank you.
Eric BelinDeChantemele	beautiful talk, thanks
Nirupama Ramkumar	Thank you for an excellent talk
Thu Le	Wonderful talk!
Jeffrey Bates	Excellent talk! Thx!
Daichi Shimbo	What a great way to start the meeting. Thank you.
David Pollock	(thumbsup)
Michelle Gumz	Wonderful presentation, thank you Dr. Scholl!
Leah Polidario	Thank you. Excellent talk.
Jami Burkhardt	Thank you!
Stephen Juraschek	Thank you for a great talke!
Tariq Qureshi	Dr. Scholl you have not mentioned 24 hour urine testing for Aldosterone which I gather is quite good in picking up PA
Edward Inscho	Nice presentation Dr. Scholl
Daniel Batlle	excellent presentation
Gilad Hamdani	Thanks for a great talk!
Curt Sigmund	The next concurrent sessions start at 10AM Central. You can choose which to watch now and the other will be available ON DEMAND later!
Addison Taylor	Excellent and timely talk
Spoorthy Kulkarni	Thanks for a great talk!
Claudia Fotzeu	Excellent. Thank you. Familial PA is redefining familial essential HTN
Tianxin Yang	Wonderful talk!
Robert Carey	Many thank for a superb review of the genetics of P
Analia Loria	Top-notch talk, congratulations!
Wataru Umishio	Excellent presentation!

Ute Scholl	24 hour urine is interesting - has traditionally been used for PA diagnosis and is now being put forward by John Funder. It's not the preferred approach according to guidelines, but certainly useful as it also measures increased aldosterone at nigh (see also link mentioned by Swapnil Hiremath above).
Ute Scholl	at *night*
Ute Scholl	Thanks for the lively discussion and again, thanks for the invitation!

Recent Advances Session 1: Results from SPRINT Sub-Studies

name	message
Chris Sampson	Welcome! Thank you for joining us. You should be hearing music play as we wait for the session to begin. If you do not, please submit a support ticket by clicking on the Request Support button located at the bottom left of the player.
Daichi Shimbo	Don't forget to click the triangle to play.
William Cushman	what triangle? I'm just hearing nice music and the AHA logo + Hypertension
Tara Chang	Good morning from Stanford!
Genevieve Gabb	snap
Bharathi Upadhya	good morning from winston salem
Suzanne Oparil	Welcome everybody!
William Cushman	(thumbsup)
Suzanne Oparil	SO
HanNaung Tun	Good morning everyone from Henry Han , @HanCardiomd
Donna Santillan	Hello from Iowa!
Atossa Niakan	Good morning from Memphis, TN
Bharathi Upadhya	Dr. Cushman -thank you
HanNaung Tun	(thumbsup)
Fathima Cader	Hi everyone!
Sabrina Scroggins	Hello and Good morning!
Curt Sigmund	Hi everyone, enjoy the session!
Mark Supiano	Good morning all from Salt Lake City
Stephen Juraschek	Good morning
Curt Sigmund	Thanks to Dr. Oparil for helping to organize this session.
Lama Ghazi	Morning from New Haven!
Karen Griffin	Welcome All! So glad you have set time aside to attend our Hypertension 2020 Scientific Sessions!
Anika Hines	Good morning all!

William Cushman	Also, in ACCORD HF was not part of the primary MACE outcome, so HF events were not adjudicated, but the event rate did appear low for the reasons mentioned.
Bharathi Upadhya	thank you , that is right
Nora Franceschini	so, the HF events were mostly low EF? Were HF with preserved EF also included?
Bharathi Upadhya	Yes all spectrum of LVEF included in assessment of ADHF - symptomatic HF with LVEF < 35% excluded at the time of randomization
Bharathi Upadhya	we are currently analyzing the data between HFpEF and HFrEF
Jackson Wright	You have me convinced.
Jan Basile	How are you doing this as I believe EF's were not measured systematically in the trial?
Nora Franceschini	awesome, thanks
Jan Basile	Prevention of HF to a goal of < 130 systolic is recommended as a Class I indication from the Heart Failure Society of American and part of the HF guidelines
Bharathi Upadhya	At the time of ADHF, we have LVEF data on more than 78% participants
Bharathi Upadhya	Yes that is true
Jan Basile	Enjoyed it, thank you!!
Bharathi Upadhya	Thank you
Bharathi Upadhya	Actually we have more information with respect to LVEF compared to other trials
Sebastiao FerreiraFilho	How was renal function?
Jan Basile	In ALLHAT, we learned that the prevention of HF was benefitted more by use of a diuretic, chlorthalidone, compared to initial use of lisinopril, and ACE inhibitor even though ACE inhibitors are used to treat HF.
Bharathi Upadhya	not much difference
Uche Iheme	Now, that is interesting
Bharathi Upadhya	Yes -that is right
Bharathi Upadhya	One thing we can see thrre diuretics arm had more BP reduction
Suzanne Oparil	You are out of time
Jackson Wright	Very nicely presented.
Bharathi Upadhya	Sorry
Bharathi Upadhya	almost done
Bharathi Upadhya	thank you Dr. Wright
Nora Franceschini	can one separate the effect of the reduction in systolic versus diastolic BP for the HF outcome?
Joni Snyder	Great talk, Bharathi, thank you!

Bharathi Upadhya	we are working on this
Bharathi Upadhya	thank you Joni - sorry for my prolong talk
Suzanne Oparil	GREAT JOB!!
William Cushman	Will it automatically proceed to next talk?
Joni Snyder	It is fine, very nice job!
Bharathi Upadhya	thank you Dr. Oprail
Lisa Fortesschramm	Very excited to see this outcome! Thank you for your presentation!
Tara Chang	Great talk!
William Cushman	(thumbsup)
Jeffrey Bates	Great talk, Bharathi!
Curt Sigmund	Applause! Thank you Dr. Upadhya
Bharathi Upadhya	thank you all
Bharathi Upadhya	i am waiting for your talk Tara
Tara Chang	(thumbsup)
Karen Griffin	Thank you, Bharathi. This is certainly useful in clinical practice.
Bharathi Upadhya	Thank you Karen
Kai Chen	Nice data
Bharathi Upadhya	thank you
Lawrence Appel	It is interesting that the BP rose in the intensive arm when the trial phase ended. The DSMB ended the trial, believing that BP in the standard arm would fall once the results became available.
Michael Ernst	interesting in that after the intervention was stopped for benefit, the BP in the standard arm did not migrate toward the intervention arm but it was the other way around...
William Cushman	BP care was turned over to usual clinical care/PCPs, who did not typically immediately apply the SPRINT intensive goal, but it seemed they often continued the same regimen the patient was on during SPRINT.
Tara Chang	Was thinking the same thing. Anecdotally, we did not purposely de-escalate BP meds post-SPRINT for those who were in the intensive group.
Genevieve Gabb	was there a difference in measurement method in followup of sprint
Junie Warrington	Were there changes in methods of BP measurement?
Bharathi Upadhya	most of them continued same
Tara Chang	No-we measured BP the same way.
William Cushman	BP measurement was the same for study visits (what Mark presented).
Bharathi Upadhya	no change in BP measurement
Junie Warrington	Thanks

Daichi Shimbo	I guess it may reflect the ongoing gap between clinical practice and trials.
Suzanne Oparil	The unavailability of free SPRINT meds may have had something to do with the BP rises after discontinuation of the trial.
Jan Basile	Mark, do you think Billy White's INFINITY trial (mean age 80) complements the results of SPRINT-MIND?
Lawrence Appel	If the BP measurement technique was the same and there was no deescaaltion, then the rise in BP in the intervention is unexplained.
Daichi Shimbo	The JAMA paper yesterday gave me great pause about this gap.
Karen Griffin	Patient adherence?
Mark Supiano	With respect to lack of adoption of intensive goal, the NHANES data just published suggests that much more work on BP control remains to be done.
Joni Snyder	Terrific presentation, Mark!
Bharathi Upadhya	Great presentation Mark
Joseph Flynn	How might these findings extend to youth/young adults with HTN? Is it a rationale to start treatment at a much younger age?
Curt Sigmund	Fantastic thanks.
Daichi Shimbo	Thanks Dr. Supiano .Great talk.
Tara Chang	Great talk and good news about the SPRINT MIND extension.
Jackson Wright	Great presentation Mark
Suzanne Oparil	Thanks much, Mark!
Karen Griffin	Wonderful presentation Mark!
William Cushman	Great presentation, Mark.
Mark Supiano	Dr. Flynn, there are pretty robust, albeit epidemiological data, to suggest that BP reduction in mid-life has later cognitive benefit
William Cushman	BP meds were no longer provided or prescribed by SPRINT clinics once the intervention was stopped.
Emily Waigi	Great presentation Dr. Supiano
Mark Supiano	Thanks all, and yes the SPRINT MIND 2020 extension will be a great addition to this body of evidence
Karen Griffin	Thank you Dr. Cushman - that answers my question.
Aimee Garza	(thumbsup)
Nora Franceschini	Did the study used a single serum creatinine measure to define CKD?
Tara Chang	I think baseline CKD was defined by a single value; the eGFR decline as an outcome had to be confirmed at 90 dayas.
Tara Chang	But let me double check that.
Nora Franceschini	you may had some people misclassified as CKD based on a single measure but the lack of interaction is reassuring

Joseph Flynn	Thanks, Dr. Supiano. Sounds like we need more data on young people.
Tara Chang	Yes - it does seem that CKD at baseline was based on single lab test.
Mark Supiano	To Dr. Basile: INFINTY was a small (n=199) group with similar impact on WMH volume benefit. Cognitive outcome was limited to a measure of executive function. Neither MCI nor dementia were adjudicated outcomes. Plus, followup was just 3 years
Jan Basile	Thanks, Mark. Thanks for the excellent presentation. I believe the data in total suggests < 130 mm Hg starting at a younger age will benefit cognition. Whether we will ever have a trial that supports this is doubtful, but important if we could get it done.
Michael Ernst	Dr. Supiano - have the cognitive outcome data been examined within the SPRINT ABPM subgroup?
Mark Supiano	Thanks, and I concur Jan. Perhaps a pragmatic trial with this objective could be conducted.
Mark Supiano	Dr. Ernst. No, the ABPM subgroup's cognitive outcomes have not to my knowledge been analyzed.
Nora Franceschini	Great talk, thanks!
Suzanne Oparil	Brilliant and VERY clinically useful presentation!!
Curt Sigmund	Thank you Dr. Chan!(thumbsup)
Suzanne Oparil	THANKS
Tara Chang	Thanks all!
Lisa Fortesschramm	fantastic!
Joshua Samuels	Great
William Cushman	The ABPM substudy many be too small to expect a very robust result.
Gilad Hamdani	Thank you!
Jeffrey Bates	Fantastic!
Atul Bali	Excellent presentation. Thank you so much!
Robert Carey	Many thanks for an excellent talk!

Angiotensin Degrading Enzymes and Their Therapeutic Potential

name	message
Chris Sampson	Welcome! Thank you for joining us. You should be hearing music play as we wait for the session to begin. If you do not, please submit a support ticket by clicking on the Request Support button located at the bottom left of the player.
Mary Haynes	thanks for the music. Glad to know everything is working, and by the way the strings are great
Mary Haynes	oops, it left
Susan Keith	My music has thankfully continued

Daniel Batlle	Welcome everyone to this virtual session , my name is Dr Daniel Batlle from Northwestern University in Chicago . I will be moderating the session this morning
Daniel Batlle	We have 3 presentations dealing with Enzymes that regulate the degradation of Angiotensin II . The first presentation will be dealing with Novel shorter ACE2 variants and will be presented by Dr Jan Wysocki from Northwestern University
Andrew South	Very much looking forward to it. Thanks for moderating Dr. Batlle.
Dulce Casarini	Greetings from Brazil
Liliya Yamaleyeva	Good morning from North Carolina! Looking forward to this session
Sarah Lindsey	Hi Liliya!
Guorui Deng	Hello Liliya!
Daniel Batlle	any questions so far ?
Andrew South	Thank you Dr. Wysocki, intriguing findings. Were you able to detect a change in kidney ACE2 expression (and subsequent changes in urinary ACE2 content/activity), rather than filtration/reabsorption of the exogenous ACE2?
Eric Lazartigues	Was this activity in the kidney significant? i saw no sign indicating it
HanNaung Tun	Morning. Nice presentation
Jan Wysocki	Thank you in the next slide we show kidney ACE2 activity
Eric Lazartigues	but this activity is extremely low. less than 3 RFU compared to higher values in previous slides
Nirupama Ramkumar	Nice presentation, Dr. Wysocki How much of kidney ACE2 is soluble versus intact (non-cleaved) ?
Jia Zhuo	why doesn't 1-740 (5) truncated ACE2 show any ACE activity in the kidney?
Eric BelinDeChantemele	the protective effects of the truncated ACE2 on blood pressure are extremely fast. is that consistent with an effects on the kidneys
Jan Wysocki	The ACE2 activity experiment was done in urine and kidney of ACE2KO injected i.v. with the rACE2. The units are different for urine RFU/ug creat/hr for urine and RFU/ug protein/hr for kidney
Jan Wysocki	Moreover, the ang 1-7 went up
Catherine LlorensCortes	When you increase ACE2 activity you not only produce increase conversion of AngII in Ang 1-7 but you also degrade apelin. Thus you decrease the hypotensive and the aquaretic effects of apelin. Have you explored the effect of rACE2 on plasma and renal apelin levels
Jan Wysocki	We think that 740 is too large to be filtered and taken up by tubules
Jan Wysocki	Good point Catherine - we did not do it

Sumit Monu	is filtration required to see the beneficial effect of rACE2 on glomerular pathology?
Brandon McFarlin	Nice talk!
Daniel Batlle	The second presentation will deal with Neprilysin inhibitors and will be presented by Mark Chappel from Wake Forest School of Medicine , North Carolina
Owen Richfield	Hi Brandon!!
Seyed Hamrahian	Would the ACE2 truncate have a role in COVID 19 associated AKI?
Jan Wysocki	Thank you
Jia Zhuo	Not sure whether the molecular wt. of truncated ACE2 proteins are larger than albumin or creatinine? If they are larger than albumin, they would be poorly filtered by the glomeruli. If they are too small after truncation, they may lose ACE2's enzymatic activities.
Jan Wysocki	Seyed, possibly and that is what we are now investigating
Jan Wysocki	You are right - if it cut too much it likely losses activity. The truncates are in the range of size of albumin but with a higher isoelectric point than albumin.
Jia Zhuo	If ACE2 is the receptors for COVID-19 virus entry into the cells, one may considered to use your truncated ACE2 peptides to test the hypothesis?
Wendy Bollag	Yes, could it be used as a decoy receptor to prevent SARS-CoV-2 entry into cells?
Jan Wysocki	The soluble truncates may compete with the receptor and act as a decoy
Jia Zhuo	Mark, greetings from Tulane and enjoy your lecture
Eric Lazartigues	Jia, this is already a fact. Several reports have confirmed ACE2 as the receptor of SARS-CoV-2 and some published studies already showed that soluble ACE2 can be used as a decoy peptide.
Jan Wysocki	Wendy, yes
Jia Zhuo	Eric, great to hear that!
Robert Speth	Can neprilysin form Ang 1-4 and 5-10 from Ang I ?
Jia Zhuo	Jan & Dan, very interesting studies and congratulations!
Jia Zhuo	Although have some questions
Jan Wysocki	Yes we have published this hypothesis about the decoy effect of soluble ACE2
Andrew South	As Dr. Wysocki noted, it remains a hypothesis. Soluble ACE2 as a treatment for SARS-CoV-2/COVID-19 has not yet been shown to be effective. Several limitations including it likely requires viremia, as no evidence that I have seen that it soluble ACE2 can be effective in the lungs.

Jia Zhuo	To see whether decoyed ACE2 proteins block COVID-19 virus entry and treat COVID-19 patients
Styliani Goulopoulou	@Dr. Chapel: neprisylin has been found in extracellular vesicles derived from the placenta and it was associated with preeclampsia. Do we know if neprilysin is transported by EVs in hypertension?
Daniel Batlle	stay tune Andrew !
Jia Zhuo	Andrew, I concur with your comments and I have not been convinced by the hypothesis yet
Catherine LlorensCortes	How an inhibitor of endopeptidase and dipeptidyl carboxypeptidase may inhibit an aminopeptidase activity
Andrew South	Eagerly, Dr. Batlle!
Mark Chappell	interesting question on EVs and enzyme components. Am aware of ACE in EVs, but not NEP
Mark Chappell	Nonspecific effects of inhibitors are not unexpected.
Mark Chappell	Bob: Ang 1-4 is a secondary clip of Ang I by NEP.
Robert Speth	thanks great presentation :)
Andrew South	Dr. Chappell, do you see sustained changes in RAS expression in the kidneys with omapatrilat, in line with that sustained increase in urinary Ang-(1-7)?
Jia Zhuo	Mark, NEPi alone has no effect on blood pressure in rats?
Styliani Goulopoulou	Dr. Chapell: back to the EVs. Here is the paper I referred to (2019). DOI: 10.1161/HYPERTENSIONAHA.119.12707
Andrew South	Very interesting paper, Dr. Goulopoulou
Mark Chappell	Andrew: Renal Ang II was decreased, with slight increase in tissue Ang 7. OMAP effect may also reflect reduced metabolism of Ang 7 by ACE.
Jia Zhuo	Mark, what are the mechanisms of NEPi for angioedema? bradyninin or kinins?
Mark Chappell	Stylaini: Thank you for citation!
Robert Speth	What about a triple therapy with a BK inhibitor?
Daniel Batlle	excellent presentation Mark
Styliani Goulopoulou	@Mark: I read this few weeks ago and I was so excited about your talk today! Thank you. Great talk as always.
Catherine LlorensCortes	What is the inhibitory potency of omapatrilat on amino peptidase A?
Mark Chappell	Hi Jia: NEPi lowers does lower but variablle in different models. Edema likely reflects BK with some role of Sub P.
Jia Zhuo	Mark, excellent talk and I learn a lot!
Kailash Pandey	In these studies is any effect on ANP and NPRA activity.
Catherine LlorensCortes	As you underlined, NEP is involved in the metabolism of apelin , is the omapatrilat effect on diuresis linked to apelin accumulation

Mark Chappell	Bob: That' interesting question on kinin antagonist which would attenuate the edema. However, increase in kinins may be beneficial - its a tough balance.
Dulce Casarini	Excellent presentation, thanks
Mark Chappell	Kailash: Yes, there should be renal effects that reflect protection of ANP/BNP
Robert Speth	does the NEP inhibitor cross the BBB?
Nirupama Ramkumar	Thanks for a great talk, Dr. Chappell. Have there been any studies on AT1R/NEP inhibitors in kidney disease ?
Mark Chappell	Catherine: Great question on apelin. We have focused on ACE2 on apelin, but NEP may play an important role of metabolism on different forms of apelin
Catherine LlorensCortes	Since NEP inhibitors such as Thiorphan are prescribed as an antidiarrheal agent, have you observed such effects in patients treated with combined AT1R antagonists and NEP inhibitors
Mark Chappell	Thank you Dulce!
Daniel Batlle	The third presentation will deal with Aminopeptidase A Inhibition and will be presented by Catherine Llorens-Cortes , from Collège de France, Paris
Aaron Trask	Nice talk, Mark!
Mark Chappell	Thank you all for great questions. My best and stay safe. -Mark
Dewan Majid	Good talk Mark!
Sarah Lindsey	Thank you, Mark!
Fatima Ryalat	Great talk Dr Chappell
Noha Shawky	Great Talk Dr Chappell
Carmen DeMiguel	Great talk Dr. Chappell!
Kailash Pandey	Mark its great talk!
Jia Zhuo	can RB150 penetrate the blood brain barrier?
Daniel Batlle	questions for Dr Llorens excellent presentation ?
Andrew South	Thank you Dr. Llorens-Cortes. Did you measure tissue levels/expression of Ang II and Ang-(1-7) in brain, heart, or kidney? Would RB150 be expected to alter risk of inflammation/fibrosis in these organs (i.e., heart failure, chronic kidney disease)?
Fernando Elijovich	Is there any generation of AngIII by aminopeptidase outside the brain?
Catherine LlorensCortes	RB150 crosses the blood brain barrier and enters the brain and the disulfide bridge is cleaved by brain reductases generating EC33
Jia Zhuo	Normally, radiolabeled angiotensin II is poorly penetrate the blood brain barrier, so most of angiotensin II in the neurons within the blood brain barrier would be endogenous. RB150 has to enter the blood brain barrier to have an effect on blood pressure?

Catherine LlorensCortes	We measured after icv injection of EC33 concomitantly with radiolabeled AngII the formation of AngIII in the hypothalamus and EC33 block completely the formation of AngIII whereas the APN inhibitor increased the half-life of AngIII by a factor 5
Dulce Casarini	This treatment decreased plasma arginine-vasopressin levels ?
Jan Wysocki	Can the inhibitor penetrate the kidney? Are the reductases in brain only? Thank you
Daniel Batlle	if not it should increase BP by degrading circulating ANG ii , is this correct Catherine ?
Catherine LlorensCortes	We measured the inhibition of renal or cardiac APA activity after RB150 treatment given by oral route during 4 weeks at the doses of 150mg/kg and no change was observed
Daniel Batlle	by impairing the degradation of ANg II I meant to say
Catherine LlorensCortes	yes, the treatment by RB150 given by oral route decreased plasma arginine-vasopressin levels
Jia Zhuo	Oral administration of RB150 would target APA not only in the brain, but also in other tissues, for example the kidney
Catherine LlorensCortes	Daniel, there is no inhibition of renal or cardiac APA activity after acute or chronic oral RB150 treatment and consequently no effect on circulating AngII levels
Daniel Batlle	in an APA KO we find that the BP is increased and the levels of circulating ANG II are increased
Catherine LlorensCortes	RB150 given by oral route during 28 days at the dose of 150 mg/kg by day has no effect on cardiac APA activity. The reason for that is that the prodrug RB150 does not inhibit APA activity since its thiol group is engaged in a disulfide bridge, and by this way it is unable to interact with the zinc atom present in the active site of APA and essential for its catalytic activity.
Catherine LlorensCortes	However, the disulfide bridge of RB150 allows to the compound to cross the blood brain barrier and enters the brain where it is cleaved by brain reductases generating EC33 which inhibits brain APA activity.
Jia Zhuo	How come? Catherine?
Fernando Elijovich	Is an additional effect of RB150 on top of an ACE inhibitor in the MI model?
Daniel Batlle	Thank you to the speakers and virtual audience for a very informative session !
Olufunke Arishe	Thank you everyone
Catherine LlorensCortes	Daniel, Pr Mitzutani has shown that in APA KO mice where brain and systemic APA are inactivated there is a slight increase of 10 mmHg in systolic blood pressure. In our case RB150 action

	predominantly acts in the brain it's a central acting prodrug of EC33
Catherine LlorensCortes	At the present time, in animals models of MI, we have not still the data of enalapril+RB150
Catherine LlorensCortes	Thank you all for great questions, best wishes from Paris

Recent Advances Session 2: Debate: Should We Lower Nighttime BP With Bedtime Dosing of Antihypertensive Medications?

name	message
Jordana Cohen	Welcome everyone to this virtual session. My name is Dr. Jordy Cohen from UPenn in Philadelphia. I will be moderating the session.
Jordana Cohen	We have an introductory talk and case from Dr. Marwah Abdallah, followed by the debate between Drs. Hermida and Hiremath. The debate includes an initial presentation by each speaker, rebuttal, and pre-recorded Q&A
Swapnil Hiremath	Good morning/afternoon everyone - thanks for being here. Look forward to the reactions and discussion
Jordana Cohen	Please use the chat to pose any questions to the speakers. When asking questions, please specify if you are posing your question to a specific speaker(s)
Chris Sampson	Welcome! As you enter the player, you should hear music playing. If you do not, please click the Request Support button. Thank you and enjoy the conference!
Ramon Hermida	Hello everyone. Glad to share this session time with all of you
Daichi Shimbo	if you don't hear music - click the triangle play button on the screen.
Daichi Shimbo	Hello, Dr. Hermida. Welcome.
Adam Bress	Excited to be here! Thanks to speakers, planners, and moderators.
Daichi Shimbo	Hi Dr. Hiremath.
Marwah Abdalla	Hello all!
Michelle Gumz	Hello from Gainesville, FL. Looking forward to this session!
Daichi Shimbo	Hi Dr. Abdalla. Welcome.
Curt Sigmund	Hello all, this will be exciting!
Brandi Wynne	Sort of excited to see this debate... Hi everyone.
Eman Gohar	Hello everyone!
Swapnil Hiremath	thanks to the organizers and Dr Shimbo and Cohen in particular
Eman Gohar	Looking forward for the session!

Lama Ghazi	Excited for this session!
Swapnil Hiremath	Hi Drs Wynne and Gumz (I had your reactions in mind for my opening)
Brandi Wynne	Ha! So excited. Let's hear it!
Curt Sigmund	We tried something different this year. We are starting this debate session with a short lecture. The formal debate will follow!
Michelle Gumz	We are on pins and needles!
Meenakshi Madhur	Hi everyone. Looking forward to the debate!
Dewan Majid	Hello Everybody!
Mohammed Nayeem	Hello Everybody!
Nirupama Ramkumar	Hi Everyone !
Sarah Melville	Hi, lots of great references in this presentation, & looking forward to the debate too, ;)
Atul Bali	Looking forward to the cons - I worry about the possibility of harm in nighttime in the 'extreme dippers' subgroup, particularly in the absence of easy availability of ABPM for a vast majority of the patients we treat.
Swapnil Hiremath	good point Dr Bali - I agree with you
Marwah Abdalla	Great point Dr. Bali! extreme dippers have increased mortality as well.
Mohammed Nayeem	What is heart rate in the night time?
Sarah Melville	ooh, wow, I didn't know that about 'extreme dippers' thought it was just a problem with non-dipping. Is there a reference that you recommend about 'extreme dipping'?
Timothy Plante	Wow! An NSAID to lower a BP?
Swapnil Hiremath	Sarah: see https://www.ahajournals.org/doi/10.1161/01.HYP.31.1.77 - extreme dipping also often means early morning surge
Marwah Abdalla	@Dr. Melville. Kario K, Pickering TG, Matsuo T, Hoshide S, Schwartz JE, Shimada K. Stroke prognosis and abnormal nocturnal blood pressure falls in older hypertensives. Hypertension. 2001;38(4):852-857. doi:10.1161/hy1001.092640
Daichi Shimbo	(thumbsup)
Ramon Hermida	One can be extreme-dipper if awake BP is too high, asleep BP too low, or both. We found than risk is associated only to too low asleep BP, but generally risk is significantly lower to dippers. Moreover, extreme-dipping is by far the lowest prevalent phenotype, around 6% of the population

Sarah Melville	Thank you, Dr. Hiremath & Dr. Abdalla. I will read those references. Nice to meet you, Dr. Abdalla, to clarify, I am not a doctor- just a clinical research associate, ;)
Ramon Hermida	Additionally, BP lowering effect with bedtime dosing is markedly associated with the baseline profile, such reduction being much greater in non-dippers compared to dippers.
Marwah Abdalla	@Timothy Plante: Dr. Hermida has published on using aspirin. Hermida RC, Ayala DE, Calvo C, et al. Administration time-dependent effects of aspirin on blood pressure in untreated hypertensive patients. Hypertension. 2003;41(6):1259-1267.
Swapnil Hiremath	@Dr Plante, also recommend reading this for ASA and BP https://journals.lww.com/jhypertension/Abstract/2019/02000/Evaluation_of_the_antihypertensive_effect_of.24.aspx in J Hypertension by Arzalluz et al 2019
Sylvia Wassertheilsmoller	Are there different effects of chronotherapy in older vs younger people?
Junie Warrington	It sounds like the focus is on wake or bedtime. What if dosing was split so that patients have a morning AND evening dose?
Swapnil Hiremath	@Dr Wassertheilsmoller: It depends! Does it have any effect before looking at subgroups I would suggest. But let's wait for the effect
Swapnil Hiremath	@Dr Warrington: that seems unwise. Adherence is usually better with once a day dosing. Smoother BP lowering as well.
Junie Warrington	I agree with the concern for adherence
Junie Warrington	thanks @Dr Hiremath
Dave Dixon	Adherence definitely a factor as disrupting patient habits with taking meds in AM can be problematic when asked to move to bedtime
Seyed Hamrahian	Dr Abdalla, thanks for the talk. In the 24hr ABPM would you use AHA cut off for night time BP or the nocturnal HTN definition you showed in the first slides in your interpretation?
Steven YAROWS	I would guess that drugs with long 1/2 lifes this does not matter and diuretics at bedtime would not be desired for people
Leo Buckley	@dldixon - agree completely!
Tariq Qureshi	I believe we should also look at the reasons for nocturnal hypertension, as many patients have OSA whihc needs treatment
Marwah Abdalla	@Dr. Hamrahian, depends on which country and guidelines apply. I personally use the 120/70 mmHg
Marwah Abdalla	@Tariq Qureshi, completely agree! My research is in hypertension and sleep and this is a very important point. OSA is prevalent especially in certain subgroups.

Junie Warrington	Sleep study?
Junie Warrington	this is my response for potential management
Jackson Wright	Marwah: Great presentation
Marwah Abdalla	Thank you Dr. Wright!
Wanpen Vongpatanasin	Great summary. Need replication by RCT in an independent group
Genevieve Gabb	how can meann 24 hour bp be higher than both mean night and day bP
James Luther	Reverse dipping = bad. Need some evidence that this can be corrected.
Swapnil Hiremath	@Dr Warrington: agree with sleep. I would also switch from HCTZ to Chlorthalidone or Indapmide (session happening concurrently)
Jan Basile	Thank you for that case and introduction!!
Junie Warrington	Great presentation!
Lama Ghazi	Loved the introduction, thank you!
Atul Bali	Such excellent presentations to choose from. I'm glad we can access the other presentations on-demand later on.
Aimee Garza	yes great presentation
Marwah Abdalla	Thank you @Jan Basile, Junie Warrington, Lama Ghazi, Atul Bali, Aimee Garza
Brandi Wynne	Has anyone really investigated other factors? Corticosteroid levels, etc?
Curt Sigmund	Thank you Dr. Abdalla!
Adam Bress	Excellent presentation, Dr. Abdalla! Thank you!
Jordana Cohen	@BrandiWynne are you referring to other factors contributing to response to chronotherapy or as an etiology of non-dipping and reverse dipping? For the latter, there are many great mechanistic studies. See Kario K. Hypertension. 2018;71:997–1009 for my favorite review https://doi.org/10.1161/HYPERTENSIONAHA.118.10971
Brandi Wynne	The former- possible contributing factors to chronotherapy.
Brandi Wynne	*as possible
Jordana Cohen	To my knowledge, we don't have mechanistic studies at this time to explain response. Please correct me if anyone knows otherwise
Brandi Wynne	@Jordy- I definitely haven't seen, but agreed, there's tons of mechanistic studies in general. I think these should be kept in mind with these chronotherapy studies.
Sarah Melville	Thank you for the recommended review, Dr. Cohen
Sebastiao FerreiraFilho	Does chronotherapy help in the control of resistant hypertension?

Swapnil Hiremath	@Brandi Wynne: definitely a good thought and worth studying. The circadian rhythm and endocrine system seem linked. Not sure any interaction with pharmacotherapy would be there. Worth studying *if* chronotherapy actually works
Brandi Wynne	@Hiremath- I think that maybe we should not always link BP-lowering and HR in CVD/KD
Meenakshi Madhur	@Brandi Wynne: My guess is that circadian rhythm and immune system are linked too and may contribute. Diet/microbiome likely involved as well.
Ramon Hermida	There are several crhonotherapy trials in resistent hypertension. This is coming shortly in my presentation
Brandi Wynne	@Meena - Absolutely.
Michelle Gumz	Highly recommend this article on the importance of circadian rhythms in human health
Michelle Gumz	Circadian disruption and human health: A bidirectional relationship Sabra M. Abbott, Roneil G. Malkani, and Phyllis C. Zee doi: 10.1111/ejn.14298
Brandi Wynne	@Hiremath- I also think that to really understand *if* chronotherapy is beneficial, we must keep these types of variables in mind.
Brandi Wynne	Thanks @ Dr. Gumz!
David Pollock	The question in my mind is whether there are subsets of pts that benefit from chronotherapy while others do not. This may be related to underlying phenotype as I think Dr. Wynne was suggesting.
Swapnil Hiremath	Excellent point @Brandi Wynne. From HARMONY and the AASK substudy, nighttime dosing did not even lower BP. So I would suggest the jury is still out there
Brandi Wynne	@Dr. Pollock- exactly! I think trying to fit everything square into all the circle holes is only going to leave more questions.
Meenakshi Madhur	@David Pollock. Agree. Maybe chronotherapy (i.e. nighttime dosing) is beneficial only in non-dippers and would not help if you are already a dipper and may be harmful if you are an extreme dipper.
Michelle Gumz	Circadian medicine should be part of precision medicine - the right drug given at the right time in the right patient
Brandi Wynne	Doing these trials without really going into it with the science and physiology in mind won't give the answers.
Amy Arnold	Potential considerations in patients with underlying autonomic impairment? Risk of night-time dosing worsening morning orthostatic tolerance?
Megan Rhoads	Well said, Dr. Gumz!
Brandi Wynne	Great comment @Gumz!

Swapnil Hiremath	@Drs Pollock and Madhur: speculation is fine and studies are appropriate. But well designed and conducted clinical trials are mandatory before making clinical decisions
Uche Iheme	@MMadhur. Good point
David Pollock	I think the population studies are telling us that we need more specific, controlled studies. Few preclinical studies examine time of day.
Ramon Hermida	HARMONY is by far the worst designed study in the field of chronotherapy, as we already published and will discussed later today. Among other issues, they used fixed clock spans for treatment, provided a wrong sample size calculation of 95 patients when the required was over 170, and they recruited only properly controlled patients in which response to treatment is expected to be low.
Brandi Wynne	@Hiremath- I think what, maybe we aren't eloquently explaining, is that you can't even interpret the trials without properly investigating the factors that could contribute to the results.
Brandi Wynne	@Pollock- You are a step ahead of me of explaining better. Thanks...
David Pollock	@Dr. Hiremath, I think this is exactly what we need. I would say this is a hypothesis, not speculation.
Brandi Wynne	@Dr. Hermida- thanks for that insight.
Ramon Hermida	In any case, HARMONY in among the 25 out of 152 studies not showing advantages of either morning or evening treatment
Ramon Hermida	Again, no one of the 152 showed significant advantages of morning treatment. We believe this should open some thoughts
Swapnil Hiremath	@Wynne: I think mechanistic studies are indeed necessary - and they complement clinical trials - but cannot help interpret them.
Brandi Wynne	Also- metabolism. I think we are really missing the mark in designing the trial around the actual question. This really brings @Dr. Gumz' comment forward.
Brandi Wynne	@Hiremath- You can try to better design the trial to at least try to answer some mechanisms. But if you aren't collecting, you can't see... Just thoughts.
Swapnil Hiremath	@Wynne: absolutley - mechanistic studies can help design better clinical trials
Sebastiao FerreiraFilho	There are patients who use antihypertensive drugs 2 times a day. In such cases, should we concentrate a higher bedtime dose?
Ross Tsuyuki	Go, Dr. Hiremath!
Ammar serawan	How can we distribute the polymedication of anti hypertension during the day
Ramon Hermida	I agree that splitting the dose reduces adherence
Atul Bali	Go #NephJC!

Styliani Goulopoulou	@Dr. Hermida: are there any differences in adherence between morning and night treatments and how this behavioral factor interacts with the benefits of chronotherapy?
Marwah Abdalla	Great talk @Dr. Hermida
Brandi Wynne	:) @Hiremath. We accept.
Curt Sigmund	Thank you Dr. Hermida. Appreciate your contribution to this conference.
Michelle Gumz	Nicely said!
Carmen DeMiguel	Great talk Dr. Hermida!
Swapnil Hiremath	@Wynne this slide dedicated to you and @gumz
Styliani Goulopoulou	I just saw the comments on dosing and adherence. Great talk, Dr. Hermida.
Brandi Wynne	Agreed. Really great talk Dr. Hermida!
Ramon Hermida	We have always been specific in instructing patients to always keep their medication at the bedside table. This markedly increases compliance and adherence, mainly if, as recommended, treatment-times are defined as upon-waking/bedtime rather than unspecific clock hours or morning/evening
Michelle Gumz	Thank you for those important details Dr. Hermida
Styliani Goulopoulou	Dr. Hermida: this must a very difficult task for both the providers and the patients, when the patients have variable schedules. Thank you for your work!
Ramon Hermida	That is the key: Bedtime is specific for each patient no matter his/her schedule
Michelle Gumz	Dr. Hermida, was there a difference in total sleep time between the awakening vs bedtime groups?
Meenakshi Madhur	But the magnitude of these changes in uric acid, LDL, etc is very very small
Swapnil Hiremath	@Dr Madhur: exactly right. Puzzled why this would occur at all. Also puzzled how you see such a huge benefit with such small changes in BP as well
Swapnil Hiremath	Especially reduction in non CV deaths (cancer?)
Atul Bali	Curious to see if systemic markers of inflammation were studied between the 2 groups (eg. hsCRP).
David Pollock	many antihypertensive drugs have effects on non-vascular/kidney cells, so maybe reducing non-CV deaths may not be surprising?
David Pollock	any measures of inflammation in the HYGEA trial?
Brandi Wynne	I think we shouldn't be scared of what we don't know...

Swapnil Hiremath	@David Pollock: would this effect vary by morning versus night? ALso this has not been reported in any trial of BP medication vs placebo.
Ramon Hermida	Sleep duration was 8.8±1.4 and 8.8±1.3, P=0.156
David Pollock	yes, the immune system has a very strong clock
Brandi Wynne	@Dr. Hermida- That's quite a bit of sleep, and consistent sleep. Is that unusual?
Swapnil Hiremath	@Wynne: not sure about your comment?
Leon Garciamartinez	The argument being presented is around the mechanism of benefit rather the lack of benefit of using nighttime dosing of antihypertensive medications
Ramon Hermida	No regularly collected info on inflammation in Hygia
Jordana Cohen	@Dr. Pollock -- could you point out other examples of trials where we see enormous non-CVD effects of antihypertensives? Would be interesting for comparison
Junie Warrington	8.8h of sleep is a lot! I wonder if there is room to stratify the data based on sleep duration? There is evidence that sleep deprivation is associated with higher BP
Brandi Wynne	@Hiremath- because I think much of your argument is based on answering the 'why'. Or at least, that's how I am interpreting it at this point.
Joseph Galley	Is there a good study looking at the effect of chronotherapy for patients with resistant hypertension?
Swapnil Hiremath	@Wynne: Not at all. I am questioning the plausibility of the findings of this study
Ramon Hermida	About sleep duration: It was restricted to >6h and <12h. A large % of participants were elderly and/or retired. Other studies also show an average duration of sleep between 8-9h in Spain
Sandra Taler	Bravo Dr. Hiremath. Well done.
Swapnil Hiremath	@Sandra Taler - thanks!
Daichi Shimbo	Really great debate. Well done to both speakers.
Ross Tsuyuki	Great presentation, thank you.
Joseph Flynn	Great points, Swap!
Adam Bress	Excellent talk, Swap! Thanks!
Brandi Wynne	@Hiremath- some really great points, and well-presented!
Edward Inscho	This has been an enlightening point/counterpoint. Thank you to all.
David Pollock	adjusting metabolism to follow a clear circadian rhythm will improve end organ health regardless of BP
Junie Warrington	Great points for both stances

Meenakshi Madhur	Agree with Brandi - great job Dr. Hiremath
Curt Sigmund	Thank you Dr. Hiremath.
Marwah Abdalla	Great presentation @Dr. Hiremath
Michelle Gumz	Great presentations, thank you!
Styliani Goulopoulou	Excellent presentations!
Sumit Monu	Great argument Dr.Hiremath
Michelle Gumz	Dr. Pollock brings up a great point, if bedtime dosing has some kind of synchronizing effect among the different tissue clocks, overall health would be expected to improve. We need better measures for this in humans.
Swapnil Hiremath	@David Pollock 'adjusting metabolism to follow a clear circadian rhythm will improve end organ health regardless of BP" Pretty Strong Statement. Quite possible - but we like to see experimental data - in humans preferably RCTs
Curt Sigmund	Dr. Cohen - Great job as moderator. Thanks so much!
Swapnil Hiremath	@David Pollock: Also: is adjusting metabolism that easy by changing medication timing?
David Pollock	@Dr. Hiremath, that's my hypothesis
Dewan Majid	Very interesting debate! Drug targeting only renin-angiotensin system, not other drugs, seems to be very important in chronotherapy!
Meenakshi Madhur	@Dr. Hiremath - changing timing of medication may help but I agree that it may not be enough to adjust metabolism. Timing of diet is probably needed too.
Ramon Hermida	Both MAPEC and Hygia indicate the benefits of bedtime trx are significantly larger for ARB and ACEI than for other medicationss
Brandi Wynne	@Dr. Madhur- but timing changes for years? I think that probably would, yes?
Michelle Gumz	The increased incidence of cancer and cardiovascular disease in shift works and other groups with chronic circadian disruption supports Dr. Pollock's hypothesis
Fernando Elijovich	Major mysteries. Thus, independent review of ABPM data seems warranted
Brandi Wynne	@Dr. Madhur- also, gut/microbiome changes..
David Pollock	There is pretty good evidence that metabolism follows a strong circadian rhythm, e.g., rest and repair at night, work during the day. @Martin Young has done a lot of this sort of work in the heart.
Meenakshi Madhur	@Dr. Wynne - Yes - time restricted feeding/intermittent fasting will likely change the microbiome/patterns in metabolism/etc

Swapnil Hiremath	@Elijovich: interesting idea
Brandi Wynne	And, especially when we consider the trial time. I just think we don't know right now. Agreed with @Hiremath's comments re: needing more studies.
Lawrence Appel	The effect sizes (benefits) in Hygia are just too large to be plausible, especially for total mortality.
Jordana Cohen	Completely agree -- TIME and BEDMED will be very interesting
Ramon Hermida	One general question: What is the justification for morning trx that no current guideline even recommends?
Brandi Wynne	Great job @Dr. Cohen!
Atul Bali	@Dr. Hermida:
Fernando Elijovich	@Appel. Agree, that is what I mean by mysteries
Swapnil Hiremath	Thank you for the comment @Lawrence Appel
Michelle Gumz	Preclinical models provide some mechanistic insight into the benefits of "bedtime" administration of valsartan from J. La
Michelle Gumz	J. Laun: DOI: 10.1080/07420528.2019.1610419 doi: 10.1080/13813455.2019.1695840.
Atul Bali	For me - All diuretics are dosed in the morning (obvious reasons). Some patients admit they missing PM doses - so I recommend AM. Lastly, I avoid bedtime doses for those with orthostatic hypotension (with the concern that they might be undiagnosed extreme dippers). What is your opinion on this matter? Any other patients that you would avoid PM dosing in?
Uche Iheme	How do the Canadians manage to do a lot more ABPMs than their U.S neighbors?
Jordana Cohen	@Dr. Hermida -- my understanding is that this is most often driven by adherence. Since many of our patients have very varying bed times, our MEMS reporting system has shown that nighttime dosing of medications seems associated with quite poorer adherence (in addition to Dr. Bali's points)
Jordana Cohen	Dr. Hermida had mentioned to us that in Vigo, the patients were instructed to put their medication at the bedside and that worked quite well. I'm very impressed -- our patients in West Philadelphia have not had such luck with this approach when indicated
Jordana Cohen	I would love some advice from the Vigo physicians on how to implement better adherence in my studies!
Swapnil Hiremath	@Cohen @Hermida: agree. Likewise adherence varies - I am happy with whatever time/system/routine works for adherence
Atul Bali	@Dr. Iheme - I wonder if this trend might be related to the narrow indications for ABPM that are covered by insurance in the US.
Uche Iheme	Good point

Swapnil Hiremath	@Iheme: In Canada also we struggle. ABPM now covered in Alberta, we are lucky in our institution in Ottawa that our centre supports the cost as the provincial health program does not support ABPM yet.
Marwah Abdalla	@Drs. Hermida and Hiremath. Love the "eternal" dilemma and frank conversation about differences in different countries
Daichi Shimbo	I want to thank Drs. Abdalla, Cohen, Hermida and Hiremath for their wonderful contributions today. We all learned.
Atul Bali	Prescribed Chlorthalidone yesterday - my patient agreed to pay the $35 for a 90 day supply (as compared to $3 for 90 days for HCTZ). Cost differences are likely a major barrier to Chlorthalidone adoption in the US.
Ramon Hermida	In Spain our studies were conducted at centers of the National Health Service. Thus, ABPM is provided for free
Marwah Abdalla	Also want to remind folks, that the chief complaint for this patient was "frequent nighttime polyuria". Does that influence your decision re diuretics at night?
Junie Warrington	I wonder, how much/how well did that patient sleep during the ABPM?
Meenakshi Madhur	@Bali - indapamide might be a cheaper option if chlorthalidone is too expensive. I switched a patient to indapamide for this very reason.
David Pollock	could polyuria simply be pressure natriuresis?
Swapnil Hiremath	@Abdalla - answering you know
Ramon Hermida	In MAPEC all patients used a wrist actigraphy at the time of each 48h evaluation. Sleep was good, at least from the point of view of activity
Atul Bali	Great point Dr. Madhur - Indapamide is on the $4 list at Walmart!
Meenakshi Madhur	@Bali - yes!
Marwah Abdalla	@swapnil :)
Ramon Hermida	I need to add that patients do not need to pay (or just a small % of the cost) for medications in Spain
Brandi Wynne	@Dr. Hermida- I think there are serious cultural differences as well. Social security nets would lower anxiety for older populations, better sleep, etc.
Junie Warrington	Yes @Wynne: It could be lifestyle differences. Americans potentially have busier lifestyles at older ages and are working at much older ages than other cultures.
Brandi Wynne	Exactly. How many elderly here are consistently sleeping 8.8hrs? Most are working well into their twilight years.
Ramon Hermida	@Brandi You might be right. Also, Hygia was performed exclusively at primary care centers, i.e., there is a long-time relation between physicians and their patients

Brandi Wynne	I know in quite a few countries, such as Iceland, they pay for their older population's complete care- from housing to health care. I have a hard time believing that wouldn't strongly contribute to results in different countries.
Swapnil Hiremath	@Wynne: Mean age in HYGIA was 60 years, so plenty of young people sleeping 8.8 hours
Lisa Fortesschramm	@brandi agreed. I don't have a single patient right now who is getting even 8 hours of sleep (santa cruz, CA). It is a serious problem.
Michelle Gumz	anecdata, as Dr. Hiremath put it, I don't know anyone who sleeps more than 8 hours a night :(
Lisa Fortesschramm	although, a few who get 7 hours say they wake rested in the morning.
Abida Zafar	Inflammation!
Brandi Wynne	@Hiremath- People here at 60- definitely not sleeping 8.8hrs per night regularly. If we are allowed to add anecdotal data like Dr. Hiremath, I can say that I also don't know a single person.
Nirupama Ramkumar	Thank you for a great discussion Dr. Hiremath and Dr. Hermida and moderating Dr. Cohen
Daichi Shimbo	wow - that was great!
Brandon McFarlin	Great discussions, thanks!
Michelle Gumz	Wonderful session! Well done!
Lisa Fortesschramm	such a great debate with excellent info presented on both sides.
Meenakshi Madhur	Thanks all - very interesting session and discussion.
Swapnil Hiremath	thanks everyone! and AHA, Drs Shimbo, Cohen and everyone for the invite. Great discussion here as well!
Junie Warrington	Great discussion! Highlights the need for more studies in the area
Sumit Monu	Great discussion. Thanks a lot.
Brandi Wynne	@Dr. Sigmund- I propose continued debates in future AHA meetings. Really enjoyed this.
Vivek Bhalla	Thank you to Drs. Hermida and Hiremath for participating in this important debate
Carmen DeMiguel	Thank you for an excellent discussion! I really enjoyed it!
Michelle Gumz	Dr. Hermida, is there a way to measure CRP in these patients now?
Junie Warrington	Seconded @Wynne
Sarah Melville	Thank you for the great presentations and for the interesting session discussion, ;)

Matthew Alexander	Great discussion. Thanks to all involved!
Vivek Bhalla	thank you, Dr. Cohen, for moderating as well.
Marwah Abdalla	Thanks to Drs. Hermida, Hiremath, Cohen and to the audience for attending our session! Great discussion.
Claudia Fotzeu	Excellent.
Jordana Cohen	Thank you to our speakers and to everyone for the very interesting discussion!!

What Level of Evidence is Needed to Change Clinical Practice? Chlorthalidone vs. HCTZ

name	message
Tara Chang	Welcome everyone! I am a nephrologist at Stanford University and will be helping to moderate the session.
Michael Ernst	Thanks in advance to the speakers. Nice to see the H vs C discussion continuing and hopefully soon with more contemporary data
James Luther	Hello- I'm Matt Luther- Nephrologist and Director of the Hypertension Center at Vanderbilt (Nashville, TN). I'll give an intro to pharmacology of these agents.
Tara Chang	Hi Matt - looking forward to you talk!
William Cushman	Thanks, Tara and Michael.
Tara Chang	Welcome, Bill - looking forward to your talk as well.
Tara Chang	Dr. Luther - would you ever use probenecid solely to prolong half life of chlorthalidone? Or would you just use higher dose of the latter?
James Luther	Tara: I think half-life of chlorthalidone is long enough that probenicid is not needed. also sequestration in RBCs may contribute to this
James Luther	*Dr. Chang.
Michael Ernst	also, regarding the significance of the carbonic anhydrase binding with chlorthalidone - CA is found in the RBC, which is why chlorthalidone partitions into RBCs and the RBC acts as a 'reservoir' for the drug
Tara Chang	Wonderful presentation!
James Luther	(thumbsup)
Paul Muntner	I agree - great presentation!
Wanpen Vongpatanasin	Enjoy it ! In the study that CTD lower nighttime BP better, was CTD given in AM or bedtime ?
Roopa Shivashankar	excellent presentation
William Cushman	I believe both in AM, but Dr. Ernst can confirm.
Michael Ernst	yes, both were given in the AM
James Luther	will post link- but since Dr. Ernst is here...
Wanpen Vongpatanasin	Thank you

James Luther	https://www.ahajournals.org/doi/10.1161/01.HYP.0000203309.07140.d3
Wanpen Vongpatanasin	I have many patients complaining that if they cut CTD to 12.5, the pills crumble. Any good tips ?
Michael Ernst	Yes out of pocket cost of chlorthalidone to the patient has gone up significantly
Tara Chang	With the long half-life of CTD, I often tell patients to take 25 mg every Monday, Wednesday and Friday instead of cutting.
Wanpen Vongpatanasin	great idea
Tara Chang	It is too bad though that the smallest dose of ctd is 25 mg.
James Luther	That is a common complaint (crumbling)- I don't have a great answer, but the minor difference by day should not make a major difference
James Luther	agree would be ideal to have a 12.5mg tab
William Cushman	We've had few complaints about difficulty splitting CTD, but it would be great for someone to make 12.5 mg.
Michael Ernst	they will 'snap' much better when done by hand rather than using a pill cutter, but patients don't always have the dexterity to do this
William Cushman	I meant in the Diuretic Comparison Project and Karen may want to comment on her THIAZIDES study.
James Luther	There is also a combination Atenolol-Chlorthalidone 50/25 tablet. I do not use, but I wonder if it would split.
William Cushman	Giving 25mg CTD MWF makes sense, but it hasn't been used that way in RCTs.
Tara Chang	azilsartan/ctd comes as 40/12.5. I use sometimes but can be $$.
Tara Chang	Yes re: MWF CTD dosing, some patients do notice that BP will fluctuate depending on whether they took or not that day, even after they should be in steady state.
James Luther	the Atenolol-Chlorthal pill is on the Kroger low cost list (near me)
Steven Smith	Dr. Cushman, on the cost issue, it strikes me that we're stuck in this rut: absent prescribing more CLD, theres no incentive for generic makes to expand dosages and increase market competition to bring prices down, but then we use cost to justify never making the switch. How to get out of this rut?
Lakshmi Chekka	Is there a plan to test the effects specifically in different race groups?
William Cushman	Yes, atenolol/chlorthaidone combo is a good option, but don't you still have to split it to get 12.5 mg?
Wanpen Vongpatanasin	Good to know , Azilsartan/CTD is very expensive, most of our insured pts complain

William Cushman	That's why we're doing DCP. If results are definitive, hopefully making more options of CTD will follow.
Gilad Hamdani	Any concerns regarding thiazides use and risk for non-melanoma skin cancers?
Wanpen Vongpatanasin	very important study indeed
Steven Smith	Yes, hopefully. But, as you mentioned, no RCT data support current use of HCTZ (25mg/d), yet 95% of patients are still prescribed it
Tara Chang	Is there CKD exclusion criteria for DCP?
Steven Smith	Looking forward to the results
William Cushman	The incidence of non-melanoma skin cancer was very low and not fatal, so CVD benefits should far outweigh. Also, skin cancer not seen in RCTs that I am aware of.
Tara Chang	Great talk Dr. Cushman; welcome Dr. Muntner!
William Cushman	Few patients on thiazides have severe CKD, but no specific Cr or eGFR exclusion.
Michael Ernst	Thanks Dr. Cushman. It will be very interesting if DCP finds a difference in outcomes. Given background use of other antihypertensives, significant BP differences will be unlikely, which may result in no differences in the hard outcomes
Tara Chang	Thank you - anecdotally I do use CTD in my patients with advanced CKD not yet on dialysis.
Ravi Nistala	Dr. Chang, is there evidence that thiazides work in advanced CKD
Tara Chang	Yes: https://www.karger.com/Article/FullText/358603
Tariq Qureshi	Dr. Chang any concern in using thiazides in lets say mild form of CKD - essentially to some extent GFR will fall with use of thiazide diuretics
Tara Chang	and Dr. Agarwal has larger RCT ongoing (CLICK trial): https://clinicaltrials.gov/ct2/show/NCT02841280
Tara Chang	I monitor the creatinine,along with Na, K. I tolerate a modest rise in SCr, so long as it then stabilizes.
Michael Ernst	Dr. Qureshi - ALLHAT reported on renal outcomes - no difference in development of ESRD between groups
Ravi Nistala	Thanks for the references
William Cushman	I looked up and atenolol/chlorthalidone does seems to come in 50/25 and 100/25 mg. Azilsartan/CTD does have 12.5 mg option.
James Luther	In our local uninsured clinics- Atenolol-Chlrothalidone is used purely due to cost issues, when "stepped up" from HCTZ. Much cheaper than the Chlorthalidone tab.
Tara Chang	I did not know atenolol-ctd cheaper than just ctd alone.
James Luther	The Chlorthalidone price has fluctuated a lot when I look- varies a lot.

Tara Chang	Dr. Muntner - in the Ontario study you discussed earlier, can you remind us what doses of each were being compared?
Paul Muntner	It varies - but a variety of sub-group analyses compared dosages.
Paul Muntner	For example, 12.5, 25, or 50 mg of chlorthalidone per day versus 12.5, 25, or 50 mg of hydrochlorothiazide per day
James Luther	Dr. Chang: at one point atenolol/Chlor was free at certain pharmacies. Currently on GoodRx it is 50% cost of just chlorthalidone tab. Nothing makes sense these days.
Karen Margolis	Just seeing this chat. We actually didn't have a lot of complaints. We sent everyone a pill splitter.
Tara Chang	Excellent, thanks Dr. Munter and all our speaker. Thanks to the audience.
Robert Carey	Great talk, Paul.
Wanpen Vongpatanasin	Excellent session, thanks all speakers for chat and presentation

Emerging tools and Analytic Approaches in Hypertension in 2020

name	message
Chris Sampson	Welcome! As you enter the player, you should hear music playing. If you do not, please click the Request Support button. Thank you and enjoy the conference!
Paul Drawz	Welcome to this AHA session on emerging tools and analytic approaches. My name is Paul Drawz. I am a nephrologist and hypertension researcher at the University of Minnesota. I'll be helping to moderate the session today.
Andrew South	Thank you Dr. Drawz, looking forward to learning.
Sebastiao FerreiraFilho	Beautiful music
Dulce Casarini	Greetings from Brazil
Sebastiao FerreiraFilho	Hello Dulce!
Paul Drawz	Welcome to Dr. Chayakrit Krittanawong
Bruce Alpert	Is there a way to enlarge slides so they are readable? The print and amount of information are substandard
Nora Franceschini	can you send us the reference for the cluster method?
Tao Yang	You can enlarge it in the options at the bottom
Susan Kunish	please click the resources button and there is a pdf of these slides you can download
Andrew South	Interesting presentation Dr. Krittanawong, thank you. Are these approaches based on Bayesian networks? Have you or others used a causal model framework to better understand these relationships?

Andrew South	To your stated limitations, I would also caution that existing biostatistical/epidemiologic biases do apply to AI/ML as well; easy to assume that they do not.
Fernando Elijovich	Rather than for prognosis or management, for which we have multiple resources and guidelines, AI should focus on questions that do not have an answer yet. An important one is the residual CV risk of treated and controlled hypertensives. That is, the study of the determinants of higher risk for the same BP if the BP is achieved with treatment, rather than spontaneous in the individual. Has there been any use of AI to address this issue?
Nora Franceschini	agree, the input data quality is also important
Shi Fang	Nice talk! Can smart watches these days facilitate the evaluation? Thanks!
Paul Drawz	Welcome to Dr. Tammy Brady
Tammy Brady	Thank you for inviting me to present on this topic
Sarah Melville	many wearables & cuffless devices not yet clinically validated though...
Tammy Brady	precisely - I will touch on this later
Sarah Melville	coool, thanks, ;)
Atul Bali	So PAT = PEP + PEP?
Atul Bali	Oops - I see the slide now
Tammy Brady	yes, thats correct :)
Mahboob Rahman	Calibration needed only once?
Tammy Brady	Depends on the device
Jennifer Pryde	Are any of these dependable during exercise stress testing?
Uche Iheme	I wonder if there will be consistency of readings between elderly and younger patients
Tammy Brady	@ Jennifer pryde: these devices are pretty sensitive to motion artifact. That said, I dont know if any have specifically been tested to show their accuracy for this purpose.
Jennifer Pryde	I see. Thank you!
Tammy Brady	great question @uche iheme. As a pediatrician I'm always interested in knowing how devices perform in children
Tammy Brady	I'm hoping that we will have validation standards to test the accuracy of devices soon to guide testing
Tammy Brady	*to guide accuracy testing
Donna Santillan	Couldn't you use the validation standards used for new blood pressure monitors for these devices?
Priyanka Solanki	What are some ways these devices can reduce barriers to access of care? Are they really expensive?

Tammy Brady	@donna santillan - I could probably give an entire talk about the need for separate validation standards for these devices - I'll touch on this in a few slides
Donna Santillan	thanks!
Tammy Brady	developing these standards has been in the works for several years because of all the nuances
Atul Bali	Dr. Brady - being a founding member of the Independent Review Committee for the Validated Device Listing, I know this topic is close to your heart. I look forward to learning from your experience.
Tammy Brady	@priyanka Solanki - pricing varies as Ive found. However, it is important to remember that every one of these devices requires an initial calibration with a cuff-BP device. WIthout this, the output will not be accurate. And the frequency of calibration varies widely
Jennifer Pryde	I apologize if you touched on this, but are arrhythmias or tachyarrhythias problematic for these devices?
Priyanka Solanki	Thank you!
Lawrence Appel	Great talk Tammy. Validation with standard cuff-based devices might be the best option now, but the optimal approach, probably impractical, is prediction of outcomes.
Tammy Brady	@Atul Bali - thanks so much. And, yes, I'm very passionate about validation!
Joshua Samuels	Well done, Tammy!
Paul Drawz	Thank you Dr Brady!
Paul Drawz	Welcome to Dr Elaine M. Urbina!
Dinesh Neupane	Great presentation, Tammy !
Jordana Cohen	Great talk, Tammy! Thank you for the overview of the mechanisms and limitations of these devices
Tammy Brady	Dr. Urbina is unable to attend during this session - she has asked me to answer any questions on her behalf.
Tammy Brady	also validatebp.org !
Daichi Shimbo	So interesting data on ABPM thresholds.
Bruce Alpert	the new ISO 81060-2, 2018/9 does NOT allow mean 6 +/-8; it continues 5+/-8
Tammy Brady	the 6 +/- 8 referred to ABPM crtieria
Paul Drawz	Thank you Dr Urbina.