Reply: Medical science is based on facts and evidence

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heterogeneous components [4]. Consequently, for such segments, it cannot be stated that CAVI₀ is superior to CAVI. In fact, CAVI is deemed to be more suitable in actual human patients over the heart to ankle pathway. A recent study by Wohlfahrt *et al.* [5] of a total of 2160 white individuals shows that no clear benefit of CAVI₀ was seen.

Soon, we will disclose some further aspects of CAVI, including the coefficients *a* and *b* contained in the CAVI formula, in a scientific publication.

Supplement:

P_s : SBP, P_d : DBP, ΔP : $P_s - P_d$

P_m : mid-pressure [defined as $P_m = (P_s + P_d)/2$]

Then, $P_s = P_m + \Delta P/2$, $P_d = P_m - \Delta P/2$

$$\begin{aligned} \frac{\ln P_s - \ln P_d}{P_s - P_d} &= \frac{\ln(P_m + (\Delta P/2)) - \ln(P_m - (\Delta P/2))}{(P_m + (\Delta P/2)) - (P_m - (\Delta P/2))} \\ &= \frac{\ln(P_m + (\Delta P/2)) - \ln(P_m - (\Delta P/2))}{(P_m + (\Delta P/2)) - (P_m - (\Delta P/2))} \\ &= \frac{\ln(P_m + (\Delta P/2)) - \ln(P_m - (\Delta P/2))}{\Delta P} \\ &= \frac{\ln(P_m(1 + (\Delta P/2P_m))) - \ln(P_m(1 - (\Delta P/2P_m)))}{\Delta P} \\ &= \frac{\ln(1 + (\Delta P/2P_m)) + \ln P_m - \ln(1 - (\Delta P/2P_m)) - \ln P_m}{\Delta P} \\ &= \frac{\ln(1 + (\Delta P/2P_m)) + \ln P_m - \ln(1 - (\Delta P/2P_m)) - \ln P_m}{\Delta P} \\ &= \frac{1}{\Delta P} \left\{ \ln \left(1 + \frac{\Delta P}{2P_m} \right) - \ln \left(1 - \frac{\Delta P}{2P_m} \right) \right\} \end{aligned}$$

By applying the second order Maclaurin expansion to $\ln(1 + \Delta P/(2P_m))$ and $\ln(1 - \Delta P/(2P_m))$

$$\begin{aligned} &\approx \frac{1}{\Delta P} \left\{ \frac{\Delta P}{2P_m} - \frac{1}{2} \left(\frac{\Delta P}{2P_m} \right)^2 + \frac{\Delta P}{2P_m} + \frac{1}{2} \left(\frac{\Delta P}{2P_m} \right)^2 \right\} \\ &= \frac{1}{\Delta P} \left\{ \frac{\Delta P}{2P_m} - \frac{1}{2} \left(\frac{\Delta P}{2P_m} \right)^2 + \frac{\Delta P}{2P_m} + \frac{1}{2} \left(\frac{\Delta P}{2P_m} \right)^2 \right\} \\ &= \frac{1}{\Delta P} \left(\frac{\Delta P}{2P_m} + \frac{\Delta P}{2P_m} \right) \\ &= \frac{\Delta P}{\Delta P P_m} \\ &= \frac{\Delta P}{\Delta P P_m} \end{aligned}$$

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There are no conflicts of interest.

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Reply: Medical science is based on facts and evidence

**Bart Spronck^{a,b,c}, Alberto P. Avolio^b,
Isabella Tan^b, Mark Butlin^b, Koen D. Reesink^a,
and Tammo Delhaas^a**

We appreciate and read with great interest Shirai *et al.*'s addition [1] to the discussion involving our study on the pressure dependence of arterial stiffness index β and cardio-ankle vascular index (CAVI) [1–4]. In the present letter, we wish to point out that Shirai *et al.*'s [1] statement that CAVI represents arterial stiffness at the 'mid pressure' requires further consideration so as to clarify the underlying logical reasoning. Furthermore, we propose that the presented clinical data [1] neither support CAVI's use of 'mid pressure', nor provide evidence for or against CAVI's or CAVI₀'s *acute* blood pressure (BP) (in)dependence.

First, we appreciate that Shirai *et al.* acknowledge the mathematical correctness of stiffness index β_0 . Stiffness index β has indeed been widely used with significant clinical impact. However, to our knowledge, no clinical study has directly compared β and β_0 in terms of acute BP dependence. Therefore, we can only conclude that *theoretically* – but based on Hayashi's *experimental* findings of an exponential arterial pressure–diameter relationship [5] – β_0 should show *less* pressure dependence than β [2].

Second, Shirai *et al.* introduce 'mid pressure' (P_m , not to be confused with *mean* BP) as a novel BP-related quantity. They show mathematically that CAVI's correction approximately corresponds to using P_m as a pressure reference point.

Subsequently and moreover, they state that P_m is the appropriate pressure metric to correct CAVI's underlying and essential measurement, the heart-to-ankle pulse wave velocity (haPWV). We respectfully disagree with this statement. haPWV is PWV measured by a foot-to-foot time delay. As we detailed in our previous letter [4] – and as already shown by Bramwell *et al.* [6] – a foot-to-foot PWV is, *by definition*, dependent on DBP [diastolic blood pressure (P_d)] [7–9]. It is the (diastolic) BP dependence of haPWV for which CAVI aims to correct. Therefore, the difference between CAVI and $CAVI_0$ is not strictly a judgement on '...whether arterial stiffness is measured at the point of P_m or of P_d '. $CAVI_0$ uses the pressure at which the essential measurement of PWV is taken (P_d), whereas CAVI uses a pressure (P_m) that is approximately related to the pressure at which the measurement is taken without consideration for the theoretical or experimental evidence for the relationship of foot-to-foot measured PWV with P_d .

Shirai *et al.* [1] present Fig. 3 of their letter as evidence for their claim that haPWV depends on P_m . However, cross-sectional data cannot be reliably used to assess an acute relationship between PWV and BP [10] for reasons which we have previously discussed [11]. In fact, Shirai *et al.* themselves previously warned that 'Several reports showed that CAVI is less dependent on BP than PWV, but these results *do not necessarily mean that CAVI is independent of BP at the time of measurement*' [12]. Although a P -value is found wanting, the figure suggests that *between patients*, haPWV relates more strongly to P_m than to P_d . This is plausible and is probably due to patients with a higher P_m having an intrinsically stiffer wall. The latter is the reason that studies on reference values commonly report stiffness measures as a function of *mean* BP [13,14], which is closely related to the 'mid pressure' (P_m) as introduced by Shirai *et al.* [1]. Mean BP is the pressure that is thought to be the one more closely related to arterial (hypertensive) *remodelling*. CAVI, however, aims to correct for the confounding effect of *acute* BP changes on PWV – not for intrinsic changes in arterial stiffness due to hypertensive arterial remodelling, which is the subject of interest rather than the confounder *per se*.

Third, we fully acknowledge that clinical data sets are sometimes small. However, a small data set should not be used to 'prove' that there is no change in a variable (CAVI in this case), a statement for which the data in this example [15] was statistically underpowered (footnote on p. 108 in [11]). Nevertheless, we would like to compliment Shirai *et al.* [15] with the design of this study, which – with a larger number of patients – would be appropriate to investigate the *acute* BP dependence of CAVI and $CAVI_0$. The (large) epidemiological dataset that Shirai *et al.* refer to (Fig. 2 in [3]) on the contrary only illustrates the *cross-sectional* relationship of CAVI/ $CAVI_0$ and age/hypertension.

In conclusion, we propose that there is no need to introduce 'mid pressure' as yet another BP-related quantity, and we hold that the clinical data provided by Shirai *et al.* cannot be used to fully assess the acute BP (in)dependence of CAVI or $CAVI_0$. We would like to emphasise that we have no issue at all with the use of CAVI or the use of the VaSera device (Fukuda Denshi Co., Ltd., Tokyo, Japan). Rather, our

article [2] aimed to propose slightly modified stiffness indices – β_0 and $CAVI_0$ – that (unlike β and CAVI) are theoretically independent of BP, but similarly easy to calculate and therefore still clinically applicable. $CAVI_0$ can be directly calculated from existing CAVI values or from underlying variables provided by the VaSera system [16] – the $CAVI_0$ equation could indeed be easily implemented into the VaSera system itself. We look forward to the publication announced by Shirai *et al.* on further aspects of CAVI.

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Conflicts of interest

There are no conflicts of interest.

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Facebook advertising for disseminating hypertension knowledge to older Chinese adults

Phillip H. Dunn and Benjamin K.P. Woo

With great interest, we read the original article by Nash *et al.* [1] discussing the use of Facebook advertising for the recruitment of patients into a blood pressure clinical trial in Australia. The study was the first to determine whether Facebook may be a useful tool to enhance blood pressure clinical trial recruitment and to ascertain the effectiveness of recruiting middle to older aged study participants through intermittent broadcast of Facebook advertisements. Participant recruitment successfully increased at two of three sites where Nash's team conducted the study. The study also found that Facebook advertising could be useful in recruiting a cohort of older participants typical of cardiovascular-related clinical trials [1]. Nevertheless, the authors suggest that the success of Facebook advertising may be location-dependent. To expand upon the study, we demonstrated similar results in a Facebook advertising for disseminating hypertension knowledge to older Chinese adults.

Health disparities facing the Chinese community can be reduced through effective health education and outreach [2]. Although e-health education has enormous potential, in-person workshops are more effective at disseminating knowledge to target older Chinese-speaking population [3,4]. In our study, we created a Facebook campaign to raise awareness and knowledge on hypertension in the Chinese community. Our advertisement included a video link, a five-character title and 26-character text body both in traditional written Chinese. Advertisements were able to be targeted towards Chinese-speaking men and women aged older than

44 years as these details were included as part of registering for Facebook. We then separated the participants into three age brackets: (1) 45–54 years, (2) 55–64 years, or (3) 65 years or older. Our study tracked the click-through rate (clicks/impressions), as defined by the ratio of users who clicked on the video link to the number of total Facebook users who viewed the hypertension awareness and knowledge advertisements. The click-through rates for the three age groups were 3.57, 8.04, and 14.71% for the age brackets 45–54 years, 55–64 years, and 65 years or older, respectively.

Our results lend support to the Nash *et al.* [1] study. Facebook advertising could be useful in outreaching to older adults in different locations. These results encourage using Facebook advertisements, in Australian or Chinese older adults, to increase participations in hypertension health-related studies. Although Facebook was successful in recruiting a cohort of participants in an older age bracket typical of developing cardiovascular diseases, our study showed that the advertisement was most effective in the 65 years or older group, with a click-through rate of 14.71%. Nevertheless, success in recruiting participants in further hypertension education may not translate into success in clinical trial recruitment. Future prospective studies should be designed to determine the effects of Facebook advertising on recruiting older Chinese for blood pressure clinical trials. Given the limited sources of language and culturally appropriate health information for older Chinese [5], future studies should also be designed to determine how to effectively promote quality e-health information online.

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