

Effects of stomach content on the breath alcohol concentration-transdermal alcohol concentration relationship

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Abstract

Introduction. Wearable devices that obtain transdermal alcohol concentration (TAC) could become valuable research tools for monitoring alcohol consumption levels in naturalistic environments if the TAC they produce could be converted into quantitatively-meaningful estimates of breath alcohol concentration (eBrAC). Our team has developed mathematical models to produce eBrAC from TAC, but it is not yet clear how a variety of factors affect the accuracy of the models. Stomach content is one factor that is known to affect breath alcohol concentration (BrAC), but its effect on the BrAC-TAC relationship has not yet been studied. **Methods.** We examine the BrAC-TAC relationship by having two investigators participate in four laboratory drinking sessions with varied stomach content conditions: (i) no meal, (ii) half and (iii) full meal before drinking, and (iv) full meal after drinking. BrAC and TAC were obtained every 10 min over the BrAC curve. **Results.** Eating before drinking lowered BrAC and TAC levels, with greater variability in TAC across person-device pairings, but the BrAC-TAC relationship was not consistently altered by stomach content. The mathematical model calibration parameters, fit indices, and eBrAC curves and summary score outputs did not consistently vary based on stomach content, indicating that our models were able to produce eBrAC from TAC with similar accuracy despite variations in the shape and magnitude of the BrAC curves under different conditions. **Discussion and Conclusions.** This study represents the first examination of how stomach content affects our ability to model estimates of BrAC from TAC and indicates it is not a major factor. [Saldich EB, Wang C, Rosen I, Bartroff J, Luczak SE. Effects of stomach content on the breath alcohol concentration-transdermal alcohol concentration relationship. *Drug Alcohol Rev* 2021]

Key words: alcohol biosensor, transdermal alcohol concentration, breath alcohol concentration estimation, stomach content, real-time assessment.

Introduction

Transdermal alcohol devices can monitor alcohol consumption continuously over extended periods of time in real-world environments, and therefore have the potential to be highly useful to researchers interested in studying naturalistic drinking behavior [see 1,2]. The transdermal alcohol concentration (TAC) that the devices record is obtained at the surface of the skin, which means TAC is a combination of the subcutaneous blood alcohol concentration (BAC), the transdermal diffusion of the alcohol and the absorption of the superficial alcohol into the TAC device [see 3–5]. Thus, in relation to BAC, TAC is delayed by the time required to get from the blood into the device [6–10],

and its concentration is altered by person-level factors, such as skin thickness and hydration, device-specific factors and environmental factors, such as ambient temperature and humidity [see 2,4,5]. This reality—that raw TAC does not straightforwardly map (either temporally or quantitatively) onto BAC—makes it difficult to directly use TAC as a meaningful quantitative indicator of alcohol levels in the body [see 11,12]. This is unlike breath alcohol concentration (BrAC), which does map well onto BAC [13] and is considered basically equivalent to BAC. Unfortunately, using breath analysers in the field requires active participation, interferes with naturalistic conditions and can produce inaccurate BrAC measurements (e.g. due to mouth alcohol while drinking). Thus, the need to passively

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obtain quantitatively- and temporally-accurate concentrations of alcohol during naturalistic drinking events may still be better met via TAC, if TAC can be reliably converted into estimated BAC/BrAC (eBAC/eBrAC).

Our research team has created the *BrAC Estimator* software, which utilises physics- and physiological-based mathematical models we have developed to translate TAC into eBrAC [4,8,14–20]. We assume the dynamics of the process described by the model are common to every person. Then, variation in the BrAC-TAC relationship across each person-, environment- and device-combination is captured by the unique parameters used in the model. There are two key parameters in the model— q_1 , the rate at which alcohol diffuses through the skin, and q_2 , the net rate at which alcohol enters and leaves the skin and is processed by the TAC device. The optimal parameter values for each person-device pairing (denoted q_1^* and q_2^*) can be obtained during an alcohol administration session where an individual wears a particular device and is monitored for both TAC and BrAC [8,14,15] or by using population-based parameter estimates [4,17–19]. Once obtained, the optimal parameter values can be used to model all drinking episodes for that person-device pair. The most recent version of the *BrAC Estimator* software combines the deterministic approaches we have incorporated into software in the past [e.g. 8,21] with population-based statistical approaches (as have been examined by others [e.g. 22]), which enables us to produce credible bands around the estimated BrAC and TAC curves [4,17–19].

This mathematical system models the diffusion of alcohol from the subcutaneous blood through the skin and into TAC device (the forward phase of the model) and allows retrieval of only BrAC (the inversion phase of the model), not further back to oral ingestion or metabolism through the stomach, gut or liver. Thus, it is not expected that drinking episode variations like stomach content will affect our models, but we have yet to systematically examine this topic.

Effects of stomach content on alcohol metabolism and BAC/BrAC

Because alcohol is typically consumed orally, its bio-availability (i.e. the amount of alcohol that reaches the bloodstream) is affected by stomach content [5,23]. Food in the stomach slows the gastric emptying rate at which stomach contents (including alcohol) are emptied into the duodenum, in which most alcohol (~80%) is absorbed into the bloodstream [5,24–27]. This slowed rate of gastric emptying has been shown

to cause the bulk of alcohol absorption to occur in the stomach at a slower rate of absorption than occurs in the duodenum [25,28] and to increase the first pass metabolism of alcohol (i.e. the amount of alcohol that is metabolised before reaching the blood [29]). This increased first pass metabolism due to stomach contents has been ascribed to the extended exposure to alcohol metabolising enzymes in the stomach [30] and to the improved ability of the liver to metabolise alcohol when it is delivered at a slower pace [31]. Even when alcohol is administered intravenously, research has shown a 30–45% increase in the rate of alcohol elimination from having food in the stomach [32,33], which similarly has been attributed to both increased activity of alcohol metabolising enzymes and increased hepatic blood flow [5,31,32], with hepatic blood flow remaining elevated for over 3 h after a meal [34].

Taken together, these studies indicate having food in the stomach when consuming alcohol slows the absorption of alcohol, reduces the amount of alcohol that reaches the bloodstream and increases the rate of elimination. These effects of stomach content on alcohol pharmacokinetics in the body are consistent with studies that show eating prior to consuming alcohol reduces BAC/BrAC peak, timing of peak and the area under the alcohol curve (AUC) [35–37]. Sadler and Fox [37] demonstrated that eating prior to drinking attenuated the BrAC peak and shortened the time to reach peak BrAC in a manner that was dependent upon the amount of food consumed, with the largest amount of food resulting in about two-thirds (69%) of the fasting peak in half the time (22 vs. 44 min). In addition, Jones *et al.* [36] found AUC was reduced by ~45–60% after eating meals of various macronutrients compared with fasting, with it taking 1–2 h longer to fully eliminate alcohol from the blood in the fasted condition.

Study aims

In this study, we examine the possibility that stomach content affects the BrAC-TAC relationship and our ability to accurately produce eBrAC. We first compare raw BrAC and raw TAC peak ratios, time of peak difference scores and AUC ratios from laboratory drinking sessions with varied eating protocols conducted by two investigators. We then examine the fit of our mathematical models as coded in our *BrAC Estimator* software. We compare the model optimisation parameter values from the calibration phase for each person-device pair across the four eating conditions. If the BrAC-TAC relationship is not altered by stomach content, q_1^* and q_2^* should be consistent across the four

conditions within each person-device pair. Lastly, we examine the eBrAC curve fit indices and summary scores from the inversion phase compared with raw BrAC.

Methods

Participants

Two of the investigators (second author Asian male, last author non-Hispanic White female) collected BrAC and TAC data in the laboratory, which was not considered to be human subjects research by the University of Southern California Institutional Review Board. Participants were of similar height (within an inch), weight (within 10 lbs; body mass index normal range) and age (within 10 years). Given the primary aim of the study was to examine within-person variation in the BrAC-TAC relationship data based on stomach content, utilising investigators ensured the accuracy of participant reporting of eating/drinking prior to arriving in laboratory.

Devices

SCRAM-CAM[®] devices (Alcohol Monitoring Systems, AMS, Littleton, CO, USA) were used to measure TAC, temperature and infrared light (a measure of adherence) at the surface of the skin. BrAC measurements were obtained with Alco-Sensor IV breath analysers (Intoximeters, Inc., St. Louis, MO, USA).

Procedure

Participants each completed four drinking sessions following 4 h of fasting: (i) no meal; (ii) half meal prior: consumed half a meal 30 min prior to drinking; (iii) full meal prior: consumed a full meal 30 min prior to drinking; and (iv) full meal after: consumed a full meal 30 min after drinking. The full meals consisted of 240 mL of water and a bagel with butter and jelly (~400 cal). The half meal prior condition included half the water and food (~200 cal). The alcohol dose was held constant at 86 mL of 80 proof alcohol, or two standard drinks, for all sessions for both participants.

Drinking sessions began in the late afternoon. Participants wore the same two TAC devices, one on each bicep, in all four sessions; this placement, as opposed to on the ankle, was selected with guidance by AMS and after pilot testing in order to increase signal strength and reliability. Devices were calibrated before drinking also in accordance with AMS recommendations. During

each session, participants took ~5 min to consume meals and 15 min to consume alcohol. BrAC and TAC readings were obtained every 10 min until BrAC returned to 0.000. To be consistent with our general laboratory alcohol administration procedure [e.g. 38,39], at 150 min after alcohol administration, participants ate a meal (in all sessions, this was a 480-cal salad with chicken and 240 mL of water). Once BrAC returned to 0.000, participants left the laboratory wearing the TAC devices, which continued to read automatically every 30 min, and proceeded with routine daily activities that did not include rigorous physical exercise (i.e. more than walking) while TAC was >0.000.

Data analysis

Raw data. Each participant had two sets of TAC data per drinking session and four drinking sessions, resulting in eight TAC-BrAC datasets per participant. We examined raw TAC:raw BrAC ratios for 'peak' and 'AUC', and we examined difference scores between 'time to peak' of BrAC and simulated TAC (sTAC), which effectively is a smoothed (i.e. filtered) version of the TAC curve produced by the *BrAC Estimator* software (see black dotted lines in Figure 2).

BrAC estimator. Each of the 16 BrAC-TAC datasets was entered into the *BrAC Estimator* software to obtain unique q_1^* and q_2^* parameter values, which were then used in the inversion phase to produce the eBrAC curve and summary scores. From the calibration phase, we compared q_1^* and q_2^* values across the four eating protocols within each person-device pair. From the inversion phase, we compared raw BrAC data points modeled as a spline function to obtain a curve [40] and eBrAC summary scores for peak, AUC and 'duration >0.000'. We used three indicators of eBrAC curve fit: percent of raw BrAC captured by the 75% credible bands of the eBrAC curve, L_2 error (the square root of the sum of the squares of the difference between the BrAC and eBrAC curves) and relative L_2 error (L_2 error normalised by the square root of the sum of the squares of the BrAC curve).

Results

Raw BrAC and TAC

Figure 1 visualises the raw BrAC and both sets of raw TAC for each of the eight drinking sessions. Raw TAC data from the two devices worn simultaneously align well in most conditions, with device differences being most notable in the full meal after condition for both

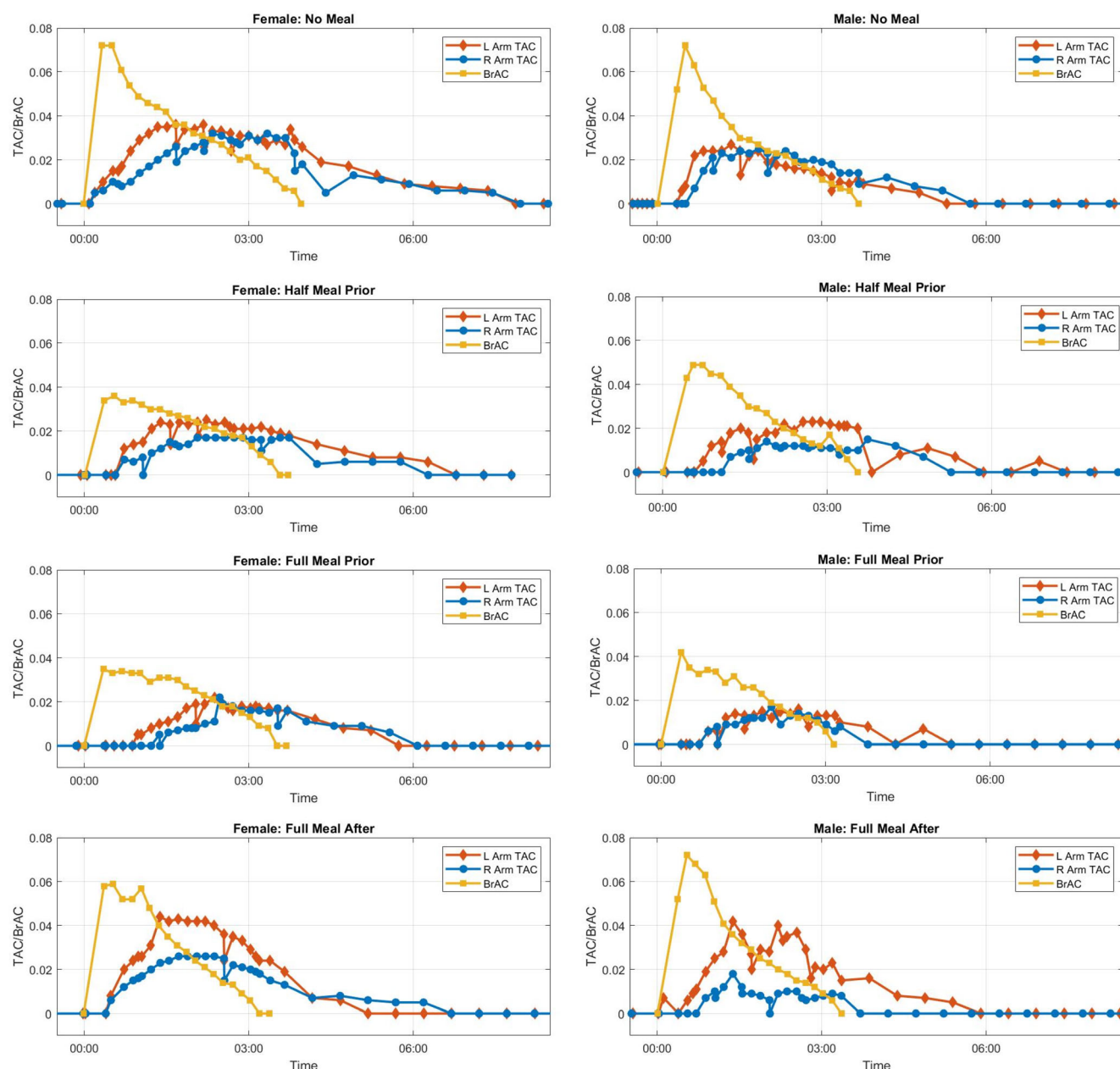


Figure 1. Raw breath alcohol concentration (BrAC) and raw transdermal alcohol concentration (TAC) curves for all eight drinking sessions.

participants (compare left and right arm TAC data of each session in Figure 1). Table 1 shows the raw BrAC and raw TAC summary scores for peak, time to peak and AUC in all 16 pairs of BrAC-TAC data, along with TAC:BrAC ratios for peak and AUC and the TAC-BrAC difference scores for time to peak. The table rows show that compared with the no meal condition, raw BrAC peak was reduced similarly for the half and full meal prior conditions (calculated as 50–51% in the female, 32–42% in the male). Raw BrAC time of peak occurred at either the 20- or 30-min post-consumption

BrAC reading in all conditions, which is prior to eating in the full meal after condition (see Table 1 for peak BrAC times). In the female participant, BrAC AUC was reduced by about one-third (39%) in both the half and full meal prior conditions and by about one-quarter (24%) in the full meal after condition compared with the no meal condition. In the male participant, BrAC AUC also was reduced by about one-third (33%) in the full meal prior condition, but by less in the half meal prior (13%) and not at all (0%) in the full meal after condition.

Table 1. Peak, time to peak and area under the curve (AUC) raw breath alcohol concentration (BrAC), raw transdermal alcohol concentration (TAC) and TAC:BrAC ratio or simulated TAC-BrAC (sTAC-BrAC) difference score for each eating condition stratified by participant

Participant	Peak level (% alcohol)						Time to peak (minutes)						AUC (% alcohol × hours)					
	Left arm			Right arm			Left sTAC-BrAC			Right sTAC-BrAC			Left arm TAC			Right arm TAC		
	BrAC	TAC	TAC: BrAC	BrAC	TAC	TAC: BrAC	BrAC	sTAC	sTAC	BrAC	sTAC	sTAC	BrAC	TAC	TAC: BrAC	BrAC	TAC	TAC: BrAC
Female	No meal	0.072	0.036	0.50	0.44	0.44	20	107	170	87	150	0.132	0.149	0.116	1.13	0.88		
	Half meal	0.036	0.025	0.69	0.47	0.47	32	125	150	93	118	0.080	0.091	0.059	1.14	0.73		
	prior Full meal	0.035	0.022	0.63	0.63	0.63	21	163	194	142	173	0.081	0.059	0.049	0.73	0.61		
	prior Full meal	0.059	0.044	0.75	0.44	0.44	32	106	124	74	92	0.100	0.112	0.082	1.12	0.82		
	after																	
Male	No meal	0.072	0.027	0.38	0.35	0.35	30	78	100	48	70	0.104	0.066	0.074	0.64	0.71		
	Half meal	0.049	0.023	0.47	0.31	0.31	33	165	147	132	114	0.091	0.083	0.041	0.91	0.45		
	prior Full meal	0.042	0.016	0.38	0.40	0.40	22	137	128	114	106	0.070	0.044	0.029	0.63	0.41		
	prior Full meal	0.072	0.042	0.58	0.25	0.25	32	130	92	97	60	0.103	0.100	0.025	0.97	0.24		
	after																	

Table 1 columns of peak TAC:BrAC ratios show they were relatively consistent within person-device pairs. In the female participant, peak ratios ranged from 0.50 to 0.75 for the left TAC device and from 0.44 to 0.63 for the right TAC device. In the male participant, peak ratios also were relatively consistent across sessions albeit somewhat lower than in the female, ranging from 0.38 to 0.58 for the left TAC device and from 0.25 to 0.40 for the right TAC device. AUC ratios also were relatively similar within person-device pair, ranging in the female from 0.73 to 1.14 for the left TAC device and from 0.61 to 0.88 for the right TAC device, and in the male from 0.63 to 0.97 for the left TAC device and from 0.24 to 0.71 for the right TAC device, with the 0.24 (from the full meal after condition) being slightly out of range. There was no clear trend in the ratio values among the eating conditions across the device pairs.

Table 1 shows time to peak sTAC had a wider range than time to peak BrAC, with both meal prior conditions delaying the peak compared with no meal, with the exception of female right TAC device. The full meal after condition either closely approximated the no meal condition (e.g. female left TAC device, male right TAC device) or fell between it and the meal prior conditions (e.g. male left TAC device), with the exception of the female right TAC device.

BrAC estimator outcomes

The first two columns of Table 2 show the q_1^* and q_2^* parameter values produced by the *BrAC Estimator* software for each dataset. There was not a clear effect of stomach content on the parameters, with values being in a similar range [0.30–2.09, with the exception of one q_1^* value of 6.00 (from the male participant's left arm no meal condition, see panel 1 of Figure 2b)] for each person-device pair across eating conditions. (Note that these scores can be magnitudes higher for some person-device pairs under varying conditions.)

The middle columns of Table 2 show the three episode summary scores. Peak BrAC and peak eBrAC matched closely, with difference scores being only >0.010 in three of the 16 datasets. Moreover, the difference between peak BrAC and eBrAC did not appear to depend on stomach content condition. The AUC difference scores also were consistently low in all datasets, with all 16 datasets below 0.020% alcohol $\times$ hours, including 11 datasets ≤ 0.010 . Finally, the duration >0.000 difference was <30 min in all datasets except one at 35 min (female, left arm, full meal after condition), including six within 10 min of each other, which was the time interval between raw

BrAC readings in our protocol. As with peak, the AUC and duration >0.000 difference scores showed no clear pattern of variation across the stomach content conditions.

The last three columns of Table 2 and Figure 2a (female) and b (male) show the eBrAC curves and fit indices. In most of the 16 datasets, the eBrAC curves mapped well onto the raw BrAC curve, and the sTAC curves mapped well onto the raw TAC curve. Goodness of fit across stomach content conditions was relatively similar, with percent of raw BrAC captured by the eBrAC 75% credible band ranging from 63 to 86% in the female and from 60 to 91% in the male. L_2 error showed the difference in the BrAC and eBrAC values was ≤ 0.020 in all but two datasets (female, left and right arms, no meal condition), and relative L_2 error showed curve fits all below 0.40, including three below 0.20 and 9 datasets in the 0.20–0.30 range. These results were consistent across the two devices worn by each participant. As with the summary scores, there was no indication the variability was linked to stomach content.

In a final set of analyses, we reran the *BrAC Estimator* software inversion phase for the three eating conditions using the q_1^* and q_2^* values obtained from the no meal condition for each of the four person-device pairs (see Figure 2c for the left arm TAC device results, which can be compared to the left columns of Figure 2a,b, and Table S1, Supporting Information, for numeric results). eBrAC curves and fits were largely consistent with fits when each session was run through the software separately, indicating the parameter values obtained in the fasting state, which is the protocol we have used in the past to calibrate the model parameters for each person-device pair, continue to produce relatively accurate eBrAC from TAC in drinking episodes with varied timing and quantities of stomach contents.

Discussion

This study examined the effect of stomach content on the BrAC-TAC relationship by comparing raw BrAC-TAC data, *BrAC Estimator* model parameters within device-person pair, and model output of eBrAC curves and summary scores. The confluence of evidence from these three approaches points to there not being a strong effect of stomach content on the BrAC-TAC relationship or on our ability to model this relationship into eBrAC. Variation in peak BrAC across our eating conditions was consistent with well-established effects of stomach content on peak BrAC [5,23], although we did not see the expected delay in peak BrAC timing from eating [37] perhaps because of differences in our

Table 2. BrAC Estimator output from calibration and inversion phases for each breath alcohol concentration-transdermal alcohol concentration (BrAC-TAC) dataset

	Parameter values			Peak level (% alcohol)			AUC (% alcohol x hours)			Duration >0.000 (hours)			Model fit indices		
	q_1^*	q_2^*		eBrAC	BrAC	BrAC-eBrAC	eBrAC	BrAC	BrAC-eBrAC	eBrAC	BrAC	BrAC-eBrAC	% BrAC captured	L_2 error	Relative L_2 error
Female															
Left arm	No meal	0.73	1.10	0.055	0.072	0.017	0.130	0.131	0.001	4.23	3.97	-0.26	79	0.023	0.308
	Half meal	0.86	1.15	0.039	0.036	-0.003	0.076	0.080	0.004	3.67	3.55	-0.12	68	0.010	0.222
	prior														
	Full meal	0.46	0.86	0.034	0.035	0.001	0.072	0.081	0.009	3.27	3.52	0.25	82	0.011	0.236
Right arm	prior														
	Full meal	1.47	1.22	0.059	0.059	0.000	0.092	0.100	0.008	2.62	3.20	0.58	80	0.011	0.175
	after														
	No meal	0.45	0.96	0.045	0.072	0.027	0.123	0.131	0.008	3.95	3.97	0.02	63	0.029	0.381
Right arm	Half meal	0.59	0.83	0.032	0.036	0.004	0.075	0.080	0.005	3.48	3.55	0.07	86	0.007	0.158
	prior														
	Full meal	0.30	0.75	0.033	0.035	0.002	0.070	0.081	0.011	3.08	3.52	0.44	77	0.018	0.392
	prior														
Full meal	after														
	No meal	0.78	0.85	0.056	0.059	0.003	0.095	0.100	0.005	2.90	3.20	0.30	80	0.010	0.157
	after														
	No meal														
Male															
Left arm	No meal	6.00	0.70	0.070	0.072	0.002	0.093	0.104	0.011	3.75	3.67	-0.08	73	0.013	0.203
	Half meal	0.56	0.95	0.040	0.049	0.009	0.084	0.091	0.007	3.43	3.55	0.12	90	0.013	0.242
	prior														
	Full meal	0.57	0.71	0.034	0.042	0.008	0.065	0.070	0.005	2.93	3.15	0.22	84	0.010	0.224
Right arm	prior														
	Full meal	1.15	1.08	0.055	0.072	0.017	0.093	0.103	0.010	3.63	3.35	-0.28	60	0.020	0.304
	after														
	No meal	1.15	0.81	0.064	0.072	0.008	0.093	0.104	0.011	3.78	3.67	-0.11	91	0.014	0.210
Right arm	Half meal	0.37	0.57	0.045	0.049	0.004	0.079	0.091	0.012	3.32	3.55	0.23	86	0.012	0.235
	prior														
	Full meal	0.97	0.54	0.032	0.042	0.010	0.060	0.070	0.010	2.68	3.15	0.47	68	0.013	0.291
	prior														
Full meal	after														
	No meal	2.09	0.30	0.063	0.072	0.009	0.086	0.103	0.017	2.90	3.35	0.45	75	0.017	0.249

The BrAC AUC output from the *BrAC Estimator* software shown here vary slightly from the BrAC AUC in Table 1 due to rounding differences. AUC, area under the curve; eBrAC, estimates of breath alcohol concentration.

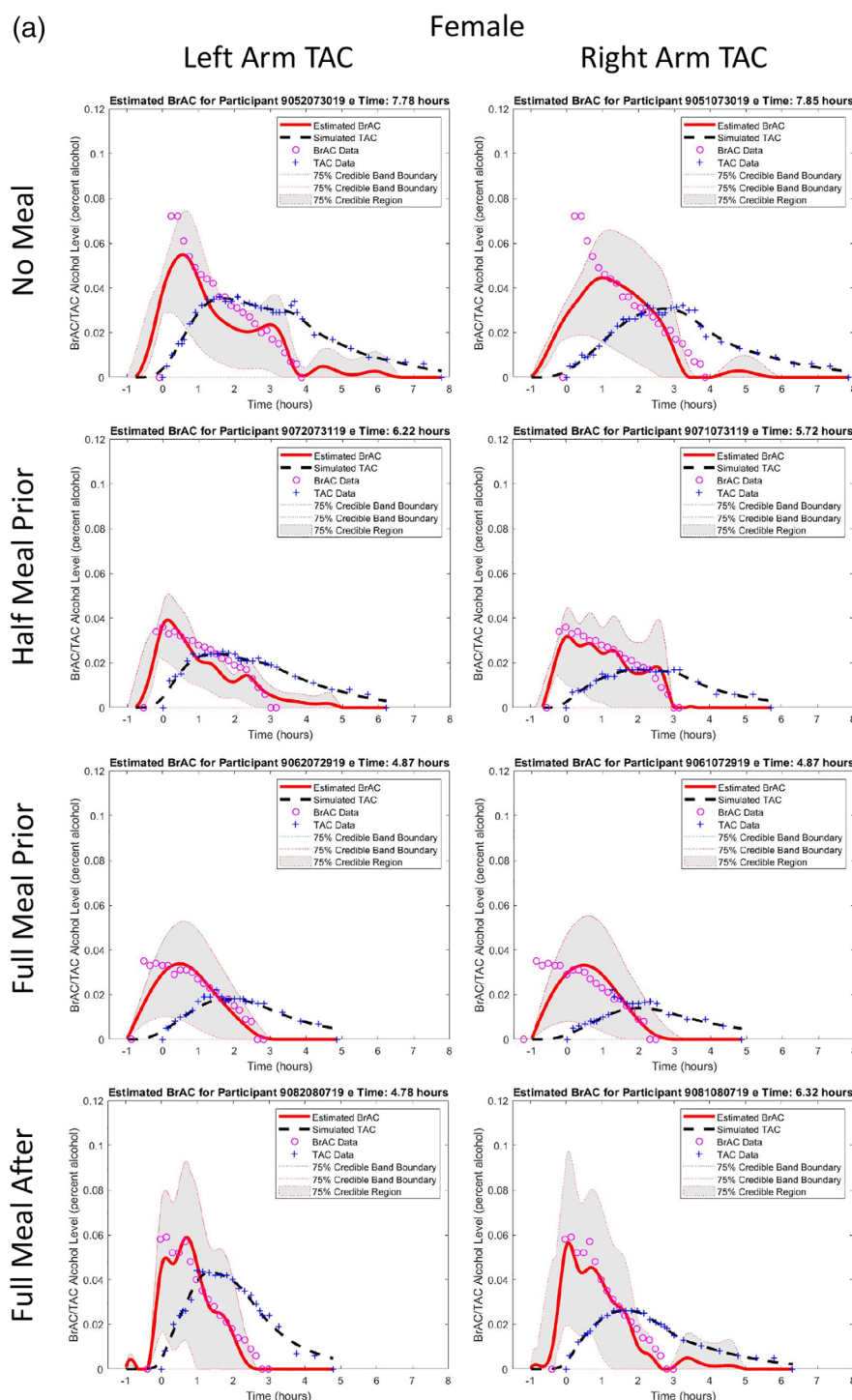


Figure 2. Estimated breath alcohol concentration (eBrAC) curve with 75% credible band and simulated transdermal alcohol concentration (TAC) curve from the BrAC Estimator software compared with raw BrAC and raw TAC measurements in all sessions for (a) the female participant and (b) the male participant, and (c) the three eating conditions for both the female and male left arm TAC device when calibrated using the no meal condition parameter values for that person-device pair.

protocol that resulted in a steep ascending limb in all of our datasets.

As expected, we observed raw TAC score variations across the two participants and their devices, but the

variability in TAC did not appear to be related to stomach content condition. Reductions in TAC peak and AUC in the meal prior conditions mapped onto reductions in BrAC peak and AUC, respectively, in

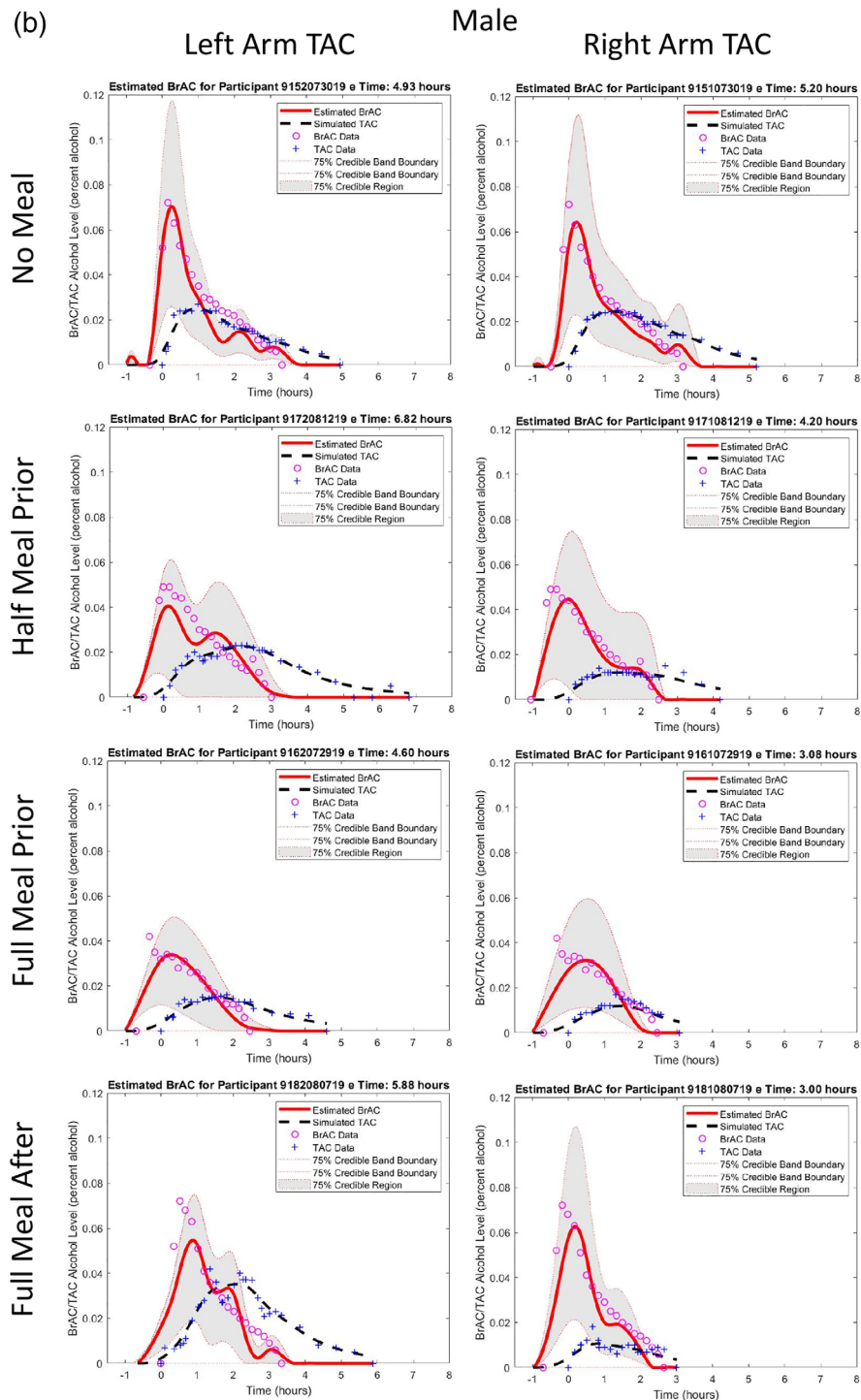
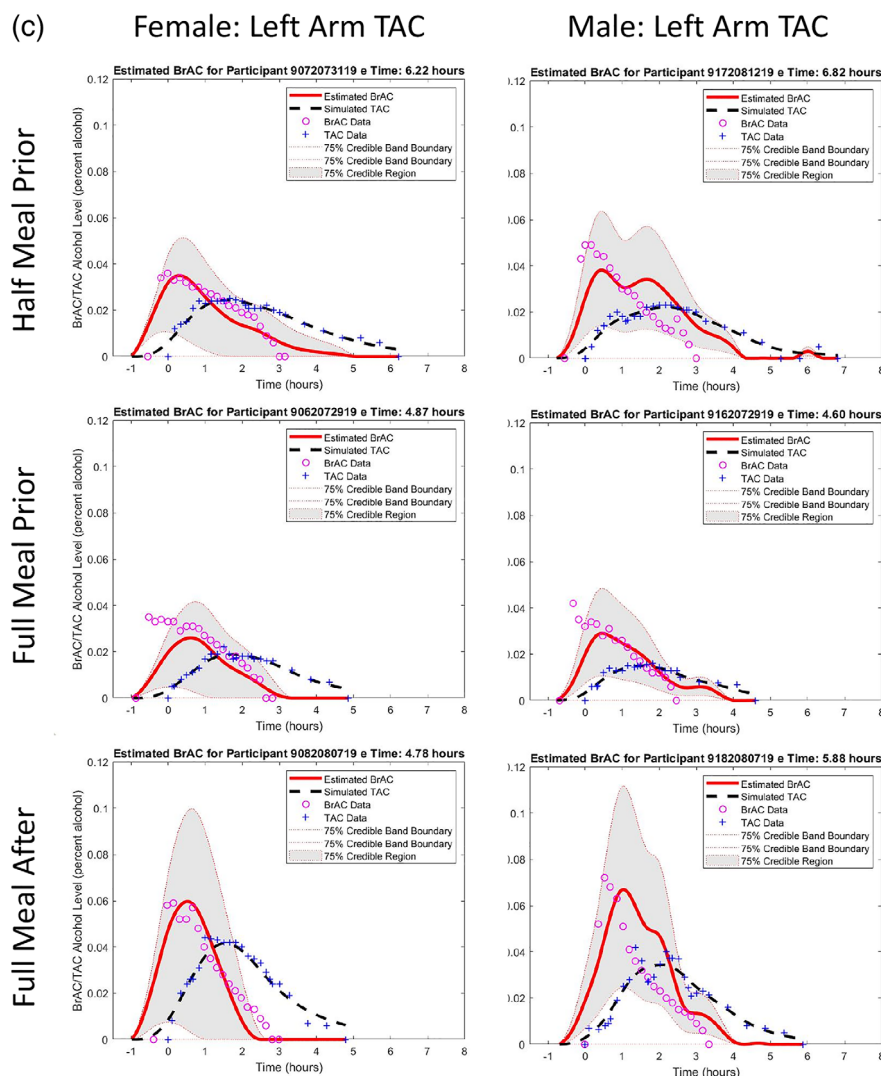


Figure 2. Continued

most of the datasets. We also observed delayed time of peak TAC (but not BrAC) in some of the meal prior datasets. However, because the TAC curves often plateaued, which is expected due to diffusion process through the skin, it can be difficult to determine both the exact peak TAC time and its importance as a single time point. This effect of diffusion, along with different timing

protocols for obtaining BrAC and TAC and use of different TAC device brands and models, also may explain some of the variability of peak BrAC-TAC lag times reported in prior studies [7,9,22]. Thus, comparing BrAC and TAC peak times may be a less meaningful indicator of how BrAC and TAC relate to one another than other summary scores, such as peak and AUC.

Figure 2. *Continued*

The most important finding of this study is that even with variations in TAC curves and TAC:BrAC ratios on summary scores across datasets for each person-device pair (including devices worn simultaneously), our mathematical models were able to produce relatively accurate eBrAC from raw TAC. The eBrAC curves accounted for variation in the shape and magnitude of the raw BrAC curves across drinking episodes, individuals, devices and stomach content conditions, and model output eBrAC summary scores matched well with raw BrAC summary scores. Our models utilise the BrAC-TAC relationship for each person-device pair over the entire BrAC and TAC curves (both from 0.000 and back down to 0.000) to convert TAC into eBrAC, representing a loop from BAC to TAC and back only to estimates of BrAC, and thus do not include modeling the absorption of alcohol from the stomach and gut into the blood. Now, beyond the physiological rationale of the model, this study

provides empirical evidence that our mathematical model is not substantially affected by BrAC variations that are due to stomach content. The results of this study add to our confidence that our models do not need to be adjusted for stomach content to produce temporally- and quantitatively-accurate eBrAC.

Given the small sample size of this study, we did not conduct statistical analyses, but future research with larger samples and sufficient power may reveal statistically significant differences across eating conditions. The effect sizes determined in these studies could then be used to understand the real-world importance of variations in stomach contents on the modeling of the BrAC-TAC relationship. This study serves as the first examination of this topic and provides initial evidence that stomach content does not appear to play a major role in the BrAC-TAC relationship or to greatly affect our ability to model TAC into eBrAC.

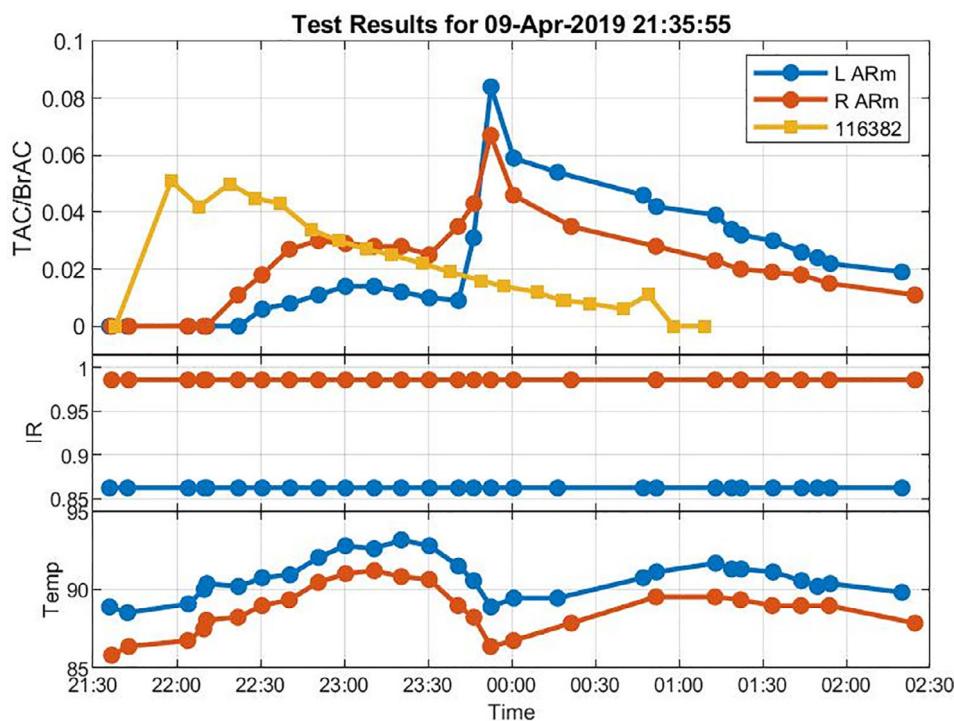


Figure 3. Raw breath alcohol concentration (BrAC) and raw transdermal alcohol concentration (TAC) curves showing an increase in TAC from 10 min of exercise half-way through descending limb of BrAC while infrared light (IR) indicates devices stayed properly adhered to the skin and ambient temperature (temp) lowered from going outdoors.

Our findings suggest that our efforts to model factors that substantially affect the BrAC-TAC relationship may be better focused on variables other than stomach content, such as skin thickness and hydration, perspiration and electrodermal activity, and/or blood flow that may substantially change this relationship (see Figure 3 as an example of TAC increasing from 10 min of running). We also note, however, that some movement (e.g. walking) and changes in ambient conditions (e.g. going outside) that occurred after participants left the laboratory in this study did not greatly affect TAC levels or our model fit, indicating a robustness of the models for a given range of routine conditions. Additional research exploring factors that will vary outside of the laboratory is necessary to improve the accuracy of our mathematical models and *BrAC Estimator* software, especially given natural drinking conditions will introduce further variation and uncertainty into the model that must be captured for TAC to become a quantitative research tool.

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and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. The authors alone are responsible for the content and writing of this paper. The authors thank Emma Ziegler for her earlier contributions to this study.

Conflict of Interest

The authors have no conflicts of interest.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Table S1. *BrAC Estimator* output using no meal, left arm parameters to produce eBrAC for each BrAC-TAC dataset.