

1 Modern fertility awareness methods: Wrist  
2 wearables capture the changes of temperature  
3 associated with the menstrual cycle  
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14 **Short title:** wrist skin temperature and the menstrual cycle  
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## 38 Abstract

39 Core and peripheral body temperatures are affected by changes in reproductive  
40 hormones during the menstrual cycle. Women worldwide use the basal body  
41 temperature (BBT) method to aid and prevent conception. However, prior research  
42 suggests taking one's daily temperature can prove inconvenient and subject to  
43 environmental factors. We investigate whether a more automatic, non-invasive  
44 temperature measurement system can detect changes in temperature across the  
45 menstrual cycle. We examined how wrist-skin temperature (WST), measured with  
46 wearable sensors, correlates with urinary tests of ovulation and may serve as a new  
47 method of fertility tracking. One hundred and thirty-six eumenorrheic, non-pregnant  
48 women participated in an observational study. Participants wore WST biosensors  
49 during sleep and reported their daily activities. An at-home luteinizing hormone test  
50 was used to confirm ovulation. WST was recorded across 437 cycles (mean  
51 cycles/participant=3.21, S.D.=2.25). We tested the relationship between the fertile  
52 window and WST temperature shifts, using the BBT three-over-six rule. A sustained  
53 three-day temperature shift was observed in 357/437 cycles (82%), with the lowest  
54 cycle temperature occurring in the fertile window 41% of the time. Most temporal shifts  
55 (307/357, 86%) occurred on ovulation day or later. The average early-luteal phase  
56 temperature was 0.33°C higher than in the fertile window. Menstrual cycle changes in  
57 WST were impervious to lifestyle factors, like having sex, alcohol or eating prior to bed,  
58 that, in prior work, have been shown to obfuscate BBT readings. Although currently  
59 costlier than BBT, this study suggests that WST could be a promising, convenient  
60 parameter for future multi-parameter fertility-awareness methods.

61 **Keywords:** Fertility awareness methods, basal body temperature, wrist skin  
62 temperature, menstrual cycle

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## 64 Clinical Perspectives

- 65 • The present study investigates an alternative, more automatic method to  
66 traditional basal body temperature (BBT) monitoring, examining how wrist-  
67 skin temperature (WST) changes across the menstrual cycle for eumenorrheic,  
68 non-pregnant women.
- 69 • We observe a similar shift in wrist skin temperature around the time of  
70 ovulation and the fertile window in the majority of participants, mirroring  
71 previously noted BBT shifts. Furthermore, whereas BBT can be prone to  
72 measurement error caused by daily activities (e.g., exercising or having a big  
73 meal prior to bed), we demonstrate WST's imperviousness to these factors.
- 74 • Our findings suggest that WST could be a promising parameter for future multi-  
75 parameter fertility-awareness methods. Easy to use and less invasive than oral,  
76 vaginal, or rectal BBT, wrist-worn wearables may empower users to become  
77 better attuned to their reproductive health and more readily identify phase-  
78 based changes in fertility-related biomarkers across the menstrual cycle.

## 79 Introduction

80 The biphasic basal body temperature (BBT) rhythm during the menstrual cycle  
81 has been reported and studied since the early 1900s (1), with the first observational  
82 study taking place in the 1960s (2). Defined as the core body temperature during the  
83 body's resting state, BBT is usually estimated by measuring one's oral, rectal, or vaginal  
84 temperature immediately upon awakening and prior to any physical activity (3). For  
85 most women, the BBT fluctuates in response to hormonal variations across the  
86 menstrual cycle. A woman's BBT reaches its lowest point (*nadir*) in a given cycle  
87 around her fertile window, just prior to ovulation and corresponding to a peak in  
88 estrogen (4). Prior work suggests that sperm can survive in the female genital track for  
89 up to six days, with higher probability of conception occurring closer to ovulation (5–  
90 7). Thus, we define the fertile window, or the timeframe in which conception can occur,  
91 as the five days leading up to ovulation and the day of ovulation itself. The probability  
92 of conception again drops sharply after ovulation, suggesting oocytes can only survive  
93 for twelve to twenty-four hours without fertilization (6,8–10). Thus, a dip in BBT may  
94 indicate imminent ovulation; after ovulation occurs, a woman's BBT typically increases  
95 as progesterone levels rise (11,12). BBT constitutes a retrospective indication of the  
96 fertile window, as one cannot identify a cycle's nadir until the subsequent post-  
97 ovulation temperature rise (13).

98 Prior research suggests that reproductive hormones are largely responsible for  
99 this biphasic shift in temperature. Estrogen, progesterone, and testosterone act  
100 directly on the warm-sensitive and cold-sensitive neurons of the preoptic anterior  
101 hypothalamus (14,15), pointing to their involvement in thermoregulation. Further,  
102 multiple studies have demonstrated that estrogen lowers the core body temperature  
103 (16–20); it, along with testosterone, both inhibit the body's heat-retaining mechanisms  
104 and accelerate the body's heat-loss mechanisms. In contrast, progesterone has the  
105 opposite chemical effect, thus increasing BBT post-ovulation (15,18).

106 Tracking one's BBT as a means of natural family planning appeals to many  
107 women. The start-up cost for participating has been historically cheap, requiring the  
108 only the purchase of a thermometer (21,22). A woman then takes her temperature  
109 each morning upon waking, recording it either electronically with an app or by hand  
110 on graph paper so that, for a given cycle, she has a chart of how her temperature has  
111 changed over time. Ideally, her temperature is taken at the same time everyday so as  
112 to minimize unintended variance due to circadian temperature shifts (23–25). In  
113 clinical settings, BBT users are often encouraged to follow the "three over six" rule to  
114 determine the start of their fertile window (2); the three over six rule suggests an  
115 upwards trend in temperature when, for the first time in a given cycle, three  
116 consecutive daily readings are higher than the six preceding daily temperatures (2,26).  
117 Some practitioners will still count this as the start of the fertile window if only 5 of the  
118 6 preceding days are lower in temperature (27). Although not an exact indicator of  
119 ovulation (28), upward shifts in BBT align with a woman's periovulatory and fertile  
120 window in most cycles (21,22,29). The relative low cost of BBT and the ability to take  
121 one's temperature at home may attract many women to BBT as a fertility tracking  
122 method.

123 While BBT requires little financial investment, its accuracy depends largely on  
124 dependable usage and remains open to interpretation error. As many researchers have  
125 noted, traditional BBT measurement cannot prospectively predict a woman's fertile  
126 window; it can only indicate retrospectively whether ovulation has occurred (21,30,31).  
127 Additionally, the method requires individuals accurately read and chart their

128 temperatures. Most women's BBT shifts only 0.28 to 0.56 °C (22,30); thus, accurate  
129 measurement requires a sensitive thermometer. Reading one's graph provides another  
130 opportunity to introduce unwanted bias into the process. If patients misinterpret their  
131 chart, they may wrongly identify their fertile window and thus reduce the method's  
132 efficacy (30,31). For this reason, it is recommended that women or couples interested  
133 in BBT attend training at a physician's office (22). Environmental factors, including  
134 sleeping in late, traveling across time zones, or alcohol consumption, can affect one's  
135 BBT, creating additional unaccounted for variance in temperature fluctuations (30).  
136 Finally, BBT may prove inconvenient for some women (21); it requires a high level of  
137 patient compliance (22), with women having to wake up at the same time daily and  
138 meticulously chart their temperatures. Failure to do so can decrease the woman's  
139 ability to correctly identify a biphasic shift in BBT when it occurs (32).

## 140 **Alternative fertility testing methods**

141 BBT does not constitute the only method for determining the fertile window,  
142 however. Some women opt instead to use at-home urine luteinizing hormone (LH)  
143 kits. Another hormone that varies across the menstrual cycle, LH rises sharply in most  
144 women anywhere from 16 to 48 hours prior to ovulation (21). This increase in LH can  
145 be detected in urine samples; specifically, LH test strips contain antibodies that bind  
146 to any LH molecules present in the urine. When the level of urinary LH is high enough,  
147 these binded complexes lead the test strip to change color (22). LH test kits range in  
148 simplicity, from single strips where users have to interpret the darkness of the LH  
149 presence line vis-à-vis a control line (e.g., Wondfo strips) to digital readers which,  
150 when fed the test strip, will indicate electronically ovulation status (e.g., ClearBlue  
151 Digital Ovulation kit). Women using the LH method often begin testing their urine on  
152 day 6 of their menstrual cycle and will continue to test for 5-9 days or until obtaining  
153 a positive indication of ovulation (33).

154 LH test kits present several potential advantages over BBT. Firstly, they  
155 constitute a prospective measure of the fertile window; because they can detect the rise  
156 in LH prior to ovulation, obtaining a positive LH test results allows a woman to know  
157 that she has 2-3 days of her fertile window left (21). Secondly, LH testing is noninvasive  
158 and highly accurate with digital readers rendering the interpretation of the fertile  
159 window less prone to human error (22). Whereas the BBT nadir aligns with the day of  
160 ovulation in only 43% of the cycles in fertile women (13), LH tests have been found to  
161 accurately predict ovulation in 90-100% of cycles (22). The test strips can be commonly  
162 found over-the-counter, with a pack of individual test strips costing only a few dollars  
163 (21,22). For some women, the method's prospective nature and increased accuracy in  
164 identifying ovulation can make urinary LH testing a more favorable alternative to BBT.

165 Urinary LH testing is not without its disadvantages, however. Whereas BBT  
166 thermometers constitute a onetime purchase, having to buy test strips for LH test kits  
167 may become expensive over numerous cycles (22). Furthermore, the LH surge can still  
168 be missed by women, even those who test daily (22). Additionally, even in those women  
169 who do manage to catch their LH surge, LH test kits can only indicate at most half of  
170 their fertile window; the days with the highest probability of conception often occur  
171 prior to a detectable LH surge (21,22). This could explain why, despite LH test's greater  
172 accuracy in detecting pending ovulation, studies have shown no difference in  
173 conception rates for women using the BBT or LH test method to track fertility (34).

174 Recent advances in technology have sought to improve upon the disadvantages  
175 of traditional BBT temping that make alternatives like LH testing more appealing.

176 Multiple wearable devices have been developed in the past ten years, claiming that they  
177 can estimate the day of ovulation by measuring temperature at various points in the  
178 body. For example, Tempdrop<sup>i</sup>, and Ava<sup>ii</sup> measure skin temperature from the armpit  
179 and the wrist respectively, while Yono<sup>iii</sup> is an eardrop with a built-in thermometer that  
180 aims to estimate core body temperature. Less invasive than traditional thermometers,  
181 these wearable devices rest on the surface of the skin and record temperature readings  
182 every few seconds to every few minutes during sleep throughout the night. They  
183 synchronize to a phone application which then automatically records and charts a  
184 woman's temperature, notifying her when the algorithm has detected a statistically  
185 significant upshift suggestive of the fertile window.

186 To date, few studies have considered the accuracy of new, wearable technology  
187 in predicting BBT shifts. There is some empirical precedence to suggest skin  
188 temperature—and not just oral or rectal temperature—may fluctuate in response to  
189 changes in the menstrual phase. Prior research, relying on skin sensors worn during a  
190 laboratory visit or at home, have shown an increase in skin temperature during the  
191 luteal phase in line with traditional BBT patterns (35). However, past studies used  
192 multiple sensors across both waking and sleeping hours; to date, none have considered  
193 whether wrist skin temperature (WST) measured during sleep alone can adequately  
194 predict menstrual phase changes.

195 With current technology, we can now empirically address many of the  
196 disadvantages affecting traditional BBT compliance and accuracy. Continuous  
197 recording of WST, for example, provides a more robust method of estimating body  
198 temperature in comparison to BBT and other methods depending on self-  
199 measurement (35). We propose conducting these measurements during sleep to  
200 capture the complete resting state and the minimum core body temperature known to  
201 occur then (3,36–40). Moreover, how WST correlates with the different phases of the  
202 menstrual cycle has not been yet elucidated. Furthermore, we examine how factors  
203 known to confound BBT measurements affect WST. If shown to be accurate, wrist  
204 wearable temperature sensors could comprise a reliable, user-friendly, and non-  
205 invasive alternative to traditional BBT (3,32–36).

## 206 **Aim of the present study**

207 The aim of the present study is to evaluate whether WST patterns correlate with  
208 the different phases of the menstrual cycle when measured continuously during sleep.  
209 In addition, we will examine the agreement between urine ovulation detection kits and  
210 classical BBT methods applied to WST. Finally, we evaluate whether WST is  
211 impervious to environmental factors known to skew traditional BBT measurements.

## 212 **Material and methods**

### 213 **Participants**

214 One hundred and ninety-four participants were recruited for an observational  
215 clinical study at the Department of Reproductive Endocrinology at the University

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<sup>i</sup> Tempdrop Ltd, Hata'asiya 11 (Hubanana Hub), Ra'anana, 43656, Israel (<http://tempdrop.xyz/>)

<sup>ii</sup> Ava AG, Raffelstrasse 26, 8045 Zurich, Switzerland (<http://www.avawomen.com/>)

<sup>iii</sup> YONO Health Inc., 4500 Great America PKWY #1038, Santa Clara, CA 95054, U.S.A. (<https://www.yonolabs.com/>)

216 Hospital Zurich, Switzerland. To be invited to participate in the study, women could  
217 not: be pregnant; have any known health-related issues; be taking medications known  
218 to affect the menstrual cycle; frequently fly across time zones; or have sleeping  
219 disorders. Further inclusion criteria were: are between 20-40 years; and regular  
220 menstrual cycles (self-reported length between 24-36 days). All study participants  
221 signed written informed consent. The ethical commission of the canton of Zurich,  
222 Switzerland approved the study protocol (approval number: KEK 170404), and the  
223 study was conducted accordingly.

## 224 **Study protocol**

225 The participants measured their temperature nightly during sleep using the Ava  
226 bracelet (Ava AG, Zürich, Switzerland), registered with the United States Food and  
227 Drug Administration as a fertility aid device. The Ava bracelet measures several  
228 physiological parameters including WST. Study participants were instructed to wear  
229 the bracelet on the dorsal side of the wrist while sleeping and on the same arm for the  
230 study's duration.

231 Ovulation day (OV) was estimated using a urine luteinizing hormone (LH)  
232 home-ovulation test (Clearblue Digital Ovulation Kit), which has been shown to have  
233 high concordance with ultrasound determination of ovulation (90-100% accurate;  
234 (41). Beginning five days after the onset of menses and extending through confirmed  
235 ovulation, women were requested to perform the LH test each morning at home. The  
236 LH test shows a smiling face indicating "peak fertility", which in turn corresponds to  
237 OV-1 in most cases (42). All participants were instructed on the usage of the tests by a  
238 trained nurse.

239 In addition to urinary tests and wearing the temperature-tracking bracelet  
240 nightly, participants also completed daily electronic diaries related to their activities  
241 and food consumption. Prior research on BBT tracking using traditional methods has  
242 found that consuming meals (43,44), drinking coffee (42), drinking alcohol (45),  
243 engaging in sexual intercourse or heavy exercise (46) in the three hours preceding sleep  
244 can significantly affect next-morning's BBT; these confounders may mask or obscure  
245 temporal shifts caused by the menstrual cycle and of primary interest to the user. To  
246 test these activities effects on WST, we had women record their participation or  
247 consumption in their daily diaries. In addition to the above factors, women also  
248 reported spotting (defined as any bleeding occurring outside the menstrual phase). A  
249 more detailed description of the covariates and their measurement units can be found  
250 in our previously published paper (47,48), which shares similar methodology but a  
251 different outcome of interest.

252 The different phases of the menstrual cycle were labeled as follows: the  
253 **menstrual phase**, beginning with menses and lasting five days; the **follicular**  
254 **phase**, beginning with the first day post-menses and lasting through OV -6; the  
255 **fertile phase**, beginning with OV -5 and lasting through OV; the **early-luteal**  
256 **phase**, beginning with OV +1 and lasting through OV +7; and, the **late-luteal phase**,  
257 beginning with OV +8 and lasting through the day prior to menses' onset.

## 258 **Data collection and data processing**

259 All data processing and analysis were performed in R (v3.3.1) and Python 3.5.  
260 The Ava bracelet continuously records WST, providing one measurement every ten  
261 seconds. To avoid variation induced by the initial drop in body temperature at the onset

262 of sleep and subsequent rise prior to waking (49,50), the first 90 and the last 30  
263 minutes of each night's data were excluded. Consistent with best practices in  
264 nonparametric modeling and to remove artificial fluctuations due to the measurement  
265 tool (51,52), temperature data were LOESS smoothed before statistical analysis. The  
266 99<sup>th</sup> (stable maxima) was chosen out of several percentiles (10, 50, 90%) to assess the  
267 correlation of WST with the different menstrual phases. There was no significant  
268 difference in a mixed effects model fit comparing data from the 99<sup>th</sup> percentile to data  
269 from the 50<sup>th</sup> or 90<sup>th</sup> percentiles, as assessed by pairwise log-likelihood tests (all  $p$ 's >  
270 0.05). The data from the 99<sup>th</sup> percentile was a significantly better fit than data from  
271 the 10<sup>th</sup> percentile ( $\chi^2(15) = 11717, p < 0.0001$ ); thus, we chose to analyze the former  
272 percentile.

273 Consistent with the three over six rule's underlying theory, we marked a shift in  
274 skin temperature when a woman's WST rose at least 0.2°C above at least 5 of the  
275 preceding 6 days and stayed elevated for a minimum of 3 consecutive days (51,53,54).  
276 Such an upward shift is useful in retrospectively confirming the occurrence of  
277 ovulation and the potential end of the fertile window. As temperature nadir was  
278 demonstrated in past BBT studies to be a prospective marker of ovulation (55), we also  
279 analyzed our WST results to see if a similar minimum temperature occurred  
280 approximating ovulation.

281 We used linear mixed effects models with random intercepts and random slopes  
282 to assess the association between WST and menstrual phases. Such models allow for  
283 the modeling of repeated measurements, accounting for correlated intra-individual  
284 and intra-cycle observations (56). Because most participants reported multiple cycles  
285 and each cycle had its own phase shift, we analyzed our data using cross-classified  
286 models; we specified that cycle numbers were nested within individual and the phases  
287 were nested within a cycle. Potential covariates previously shown to impact BBT were  
288 collected from participants' daily diary reports and assessed for their effect on WST  
289 across the menstrual cycle using similar multi-level, cross-classified models as  
290 described above. Significant covariates were included in the final multivariate multi-  
291 level model based on previously reported or potential clinical and practical relevance.  
292 Where appropriate, mean WST and its standard deviation are reported in text. For  
293 each model, unstandardized b-coefficients and their standard errors are reported in  
294 Table 1, 2, or 3.

## 295 **Results**

### 296 **Descriptive statistics of the study population**

297 Overall, 793 menstrual cycles were recorded across 194 study participants. In  
298 keeping with recommendations for best performance in fertility prediction algorithms  
299 (30,42–45), we excluded data from 186 cycles where participants reported  
300 measurements and synchronized their WST to the app less than 80% of the days  
301 between the fertile window and the early luteal phase. This left a reduced sample of  
302 603 cycles across 159 participants. We also restricted our sample to participants with  
303 a confirmed ovulation, as detected via LH test; while an interesting extension of  
304 wearable technology, tracking potential anovulatory cycles is beyond the scope of the  
305 current study. Removing 170 cycles without confirmed LH surges left us with a final  
306 sample of 437 cycles across 136 participants; the average number of cycles per user in  
307 our sample was 3.21 (S.D.=2.25). Participants had an average age of 33.66 (S.D.=3.86)  
308 and an average BMI of 22.97kg/m<sup>2</sup> (S.D.=3.68). The average cycle length for the final  
309 sample was 28.84 days (S.D.=7.02).

## 310 **Skin temperature rhythm during the menstrual cycle**

311 We detected a shift in skin temperature in 82% of the cycles. The majority of  
312 detected temperature shifts (86%) took place on or after the ovulation day (Figure 1).  
313 The choice of threshold at which the temperature shift occurred altered the  
314 aforementioned numbers minimally (e.g., setting the temperature threshold at 0.15°C  
315 yields 88% and 84% respectively). None of the participants had exclusively  
316 monophasic temperature patterns nor temperature shifts occurring exclusively before  
317 ovulation (for participants with more than one cycle).

318 Occurring mostly prior to ovulation, the lowest temperature in a given cycle was  
319 often observed outside the fertile window. Only in 41% of the 357 cycles was the nadir  
320 detected within the fertile window (OV-5 to OV; see Figure 2). Twelve percent of cycles  
321 showed a WST nadir occurring after ovulation, while the remaining 47% had the lowest  
322 WST reading prior to the fertile window. In sum, the majority (88%) of the biphasic  
323 cycles in our study exhibited a WST nadir prior to ovulation.

## 324 **Quantification of The Change in Skin Temperature Across the Menstrual** 325 **Phases**

326 Consistent with our hypothesis and patterns in traditional BBT tracking,  
327 average WST during the menstrual phase (M=35.32°C, S.D.=0.71) was significantly  
328 lower than the average WST during the early-luteal (M=36.04°C, S.D.=0.69;  
329  $t(4.05)=10.53$ ,  $P<.001$ ) and late-luteal phases (M=35.70°C, S.D.=0.63;  $t(3.83)=12.37$ ,  
330  $P<.001$ ). In addition, women had significantly lower WST (M=35.23 °C, S.D.=0.67),  
331 on average, in their fertile phase compared to their menstrual phase WST (see Table  
332 1).

## 333 **Influence of BBT-documented covariates on WST**

334 Whereas prior research has found BBT readings and temperature shifts can be  
335 skewed by environmental factors (11,51,53,57–59), our findings suggest WST is robust  
336 to these confounders. For each covariate, we ran a separate multivariate, multi-level  
337 model predicting temperature in the 99<sup>th</sup> percentile based off phase and that covariate.  
338 The main effects of phase shift describe above remained significant, even when  
339 controlling for covariates. Spotting, age, and having coffee or exercising in the three  
340 hours preceding sleep did not significantly affect WST (see Table 2). Although a  
341 woman with a higher BMI was significantly more likely to have a lower WST, the  
342 direction and magnitude of menstrual phase shifts on WST remains unchanged.  
343 Having sex and eating a large meal in the 3 hours before bed were also significantly  
344 associated with increases in nightly WST; however, the effect of menstrual phase on  
345 WST remained significant. Finally, the effect of the menstrual cycle on WST was  
346 significant even when controlling for drinking 5 or more units up to three hours before  
347 bed. For the full model statistics, please see Table 2.

348 Finally, we entered all the significant covariates into a full model with phase  
349 effects to further ensure the robustness of our hypothesis. As before, WSTs in the early-  
350 and late-luteal phases were significantly higher than WST in the menstrual phase, over  
351 and above the effects of any potential covariates (see Table 3). Our findings suggest  
352 biphasic shifts in WST across the menstrual cycle are detectable regardless of  
353 individual behavior or activities prior to sleep, a marked difference from potential  
354 confounds plaguing traditional BBT readings.

## 355 **Discussion**



356 In this study, a biphasic skin temperature pattern was identified in 82% of  
357 cycles. In addition, the nadir skin temperature did not provide a robust prospective  
358 estimation of ovulation. We observed the utility of the skin temperature as a  
359 retrospective confirmatory marker for ovulation in 86% of the cycles where a biphasic  
360 pattern was observed. Finally, we observed the robustness of wrist skin temperature  
361 measurements to environmental factors, including alcohol, coffee, exercise, food, and  
362 sex.

363 Our findings are consistent with evidence from traditional BBT studies,  
364 suggesting wrist temperature measurements tap into the same underlying mechanism.  
365 The occurrence of a monophasic, temperature pattern in ovulatory cycles in 18% of the  
366 regular ovulatory cycles corresponds to the range (0-20%) found in other studies that  
367 confirm ovulation via serum hormonal levels, ultrasound, or pregnancy (11,51,53,57–  
368 59). In our study, the proportion of cycles with retrospective ovulation confirmation by  
369 virtue of a temperature shift matches those of earlier BBT studies (22,30).  
370 Furthermore, the magnitude of the observed temperature shift in our study  
371 ( $\Delta WST_{menstrual-early\ luteal} = 0.33^{\circ}\text{C}$ ) falls within the observed range (0.28°C - 0.56°C)  
372 seen in classical BBT studies (11,51,59,60). Finally, the range of days in which the shift  
373 can occur varied broadly for both this study and previous studies (51,53,54).

374 The BBT nadir is reported to be indicative of the ovulation day and has been  
375 identified within one day of ovulation in 33-75% of the cycles in prior studies (61). In  
376 this study, a nadir was identified in 41% of the cycles within the fertile window.  
377 Although seemingly low, it is not inconsistent with the variability of BBT nadirs found  
378 in prior studies, with temperature shifts occurring as early as 8 days prior to and 4 days  
379 post ovulation (11). BBT nadirs have been found to differ from LH peaks in 55-70% of  
380 cycles (62,63). While the initial rise in progesterone levels has been shown to occur  
381 consistently around ovulation and almost never earlier than a day before ovulation,  
382 estrogen levels are much more variable (64). This could explain the more consistent  
383 observation regarding temperature elevation (associated with progesterone rise) and  
384 much less consistently the temperature decrease (associated with estrogen rise).

385 Although we estimated ovulation's occurrence via an at home LH tests, we did  
386 not confirm it in-lab via reproductive hormone levels or an ultrasound. The number of  
387 cycles with a monophasic pattern might be due to: (a) a false positive urine LH test; (b)  
388 misinterpretation or non-compliance of the user; or, (c) no (detected) shift in wrist skin  
389 temperature despite ovulation. We excluded 170 cycles out of 793 total (21%) due to no  
390 user-confirmed LH peak. This could hint towards user compliance issues with home  
391 urine tests, misuse of the device, unreliable monitors, or insufficient hormonal  
392 variation due to health conditions (33). Aside from an ultrasound, currently there are  
393 no consensus on the biomarkers for anovulation. The hormonal profile that constitutes  
394 an anovulatory cycle remains disputable, and the algorithms employed give varying  
395 rates of anovulatory cycles (3-19%; 65). A false positive rate remains an open point for  
396 future research with ultrasound verification of ovulation as a reference.

397 One of the strengths of the skin temperature method using a wearable device  
398 compared to the oral, vaginal, or rectal BBT method is the continuous measurement  
399 during the night and the ease of providing automatic detection of the shift by computer  
400 programs or smartphone applications (e.g. cycle tracking applications). This renders  
401 the measurements less susceptible to measurement errors (e.g. different waking time)  
402 and misinterpretation of the results. Similar to other wearables measuring  
403 physiological parameters, the device used in this study requires the user to sync it to  
404 the phone application. We excluded data from 186 cycles in our study due to user non-

405 compliance on 20% of the days in a given cycle (e.g., not syncing 6 days out of a 28 day  
406 cycle); it is conceivable that this compliance issue could decrease or increase in the  
407 general population depending on the device used to measure WST (e.g., one would  
408 expect the compliance to increase if the device were to automatically sync once wireless  
409 internet or a Bluetooth connection is available without the user's involvement). In this  
410 study the individuals were required to measure LH using urine tests, fill in a daily  
411 survey, and they were blind to the measurement of the device. It is plausible that in the  
412 real-world scenarios observing the daily progression of the physiological parameters  
413 and predictions would motivate the user for further compliance. Other current  
414 methods of fertility tracking are not impervious to similar limitations. Women who do  
415 not take their BBT measurements at precisely the same time daily or who miss several  
416 days in a given cycle may less easily detect a biphasic temperature shift (22). Similarly,  
417 women using LH tests who skip a day of urinary testing run the risk of missing the only  
418 indication of a LH surge and impending ovulation (33). Thus, it remains an empirical  
419 question for future studies whether women would have greater compliance using a  
420 less-invasive method like WST than using LH testing or traditional BBT.

421 On a related note, future studies may also consider whether users find WST  
422 fertility tracking less burdensome and inconvenient than BBT. Traditional BBT  
423 methods require women wake up several hours before rise to take their temperature  
424 (21). Indeed, when asked about the burden associated with BBT methods, most women  
425 in a prior study found the method cumbersome; only 15% of patients described BBT  
426 procedure as having "no burden" (53). Because wearable devices, like the one used in  
427 our study, measure WST continuously throughout the night, they alleviate the need for  
428 users to wake up early. It follows then that they may be perceived by users as being  
429 less burdensome and/or more convenient. However, this is an empirical question and  
430 one that remains to be tested. It may be that the need to sync the device with a phone  
431 daily proves similarly burdensome as taking one's vaginal, oral, or rectal temperature  
432 daily. Future studies could improve upon our findings, by exploring the potential ease  
433 of use and convenience that WST may offer over traditional BBT fertility tracking.

434 A second novel strength of wrist-based skin temperature measurement in  
435 fertility tracking appears to be its imperviousness to environmental factors. We show  
436 that wrist-based wearables are sensitive enough to pick up phase-based shifts in  
437 temperature, over and above any changes that may be due to having sex, food or  
438 alcohol consumption. This presents an advancement in fertility awareness  
439 temperature tracking, allowing women increased accuracy in ovulation prediction  
440 without having to change pre-bedtime habits.

441 Ovulation tracking methods currently cost from ten to several hundred  
442 American dollars, depending on the underlying technology (22). The calendar and BBT  
443 methods represent the lower spectrum of this price range while multi-parameter  
444 devices (such as the one employed in this study) and digital Estrogen/LH measuring  
445 devices occupy the upper range. Each of the mentioned methods have advantages and  
446 disadvantages in terms of cost, convenience, being prospective, and accuracy. Further  
447 studies comparing current methods on the market will aid the user to decide which of  
448 these methods offer a compelling case for their needs.

449 In addition to being reusable, multi-parameter devices may also offer women  
450 insight into more of their fertile days than OPKs (46,66). Although OPKs can  
451 prospectively predict the fertile window (21,22), they provide only a 12-48 hour  
452 advanced notice that ovulation may be about to occur (21). Multi-parameter devices  
453 have the potential to prospectively predict more of the fertile days (46,66). While the

454 current study examined the confirmatory presence of a shift in WST over the fertile  
455 window, when paired with more physiological parameters (e.g., pulse rate (46)) and  
456 more sophisticated statistical methods (e.g., machine-learning), devices measuring  
457 multi physiological parameters can learn an individual woman's typical cycle  
458 physiological variation and use that to detect more of her fertile days. Furthermore,  
459 this information can be made easily readable and available via a phone application.  
460 This technology could be combined with OPKs for further tuning. For example, the  
461 application would indicate the approach of the fertile window, allowing women to  
462 better predict when to begin urinary LH testing. Using both methods together, women  
463 could better identify the highest fertility days (missed by LH testing alone) and confirm  
464 that ovulation took place. Combining fertility awareness methods is widely seen as the  
465 most effective way to track fertility, with numerous researchers suggesting  
466 incorporating newer technological advances to better identify the full fertile window  
467 (22,67,68). Future studies should explore the successful conception rates of WST  
468 devices used in conjunction with other methods; it may be that this technological  
469 advance on traditional BBT provides the prospective window necessary to take  
470 advantage of the highest fertile days.

## 471 **Conclusion**

472 In this study, we demonstrated that the rhythm of skin temperature during  
473 menstrual cycle as measured by a wrist worn wearable shows a biphasic pattern in 82%  
474 of the cycles, which is comparable to the results obtained in prior studies using BBT.  
475 Consequently, daily skin temperature measurements taken during the night with  
476 today's wearable sensor technology could be a potential alternative for the oral, rectal,  
477 or vaginal BBT method. However, by itself, and in agreement with the BBT method,  
478 WST did not capture all ovulation events, and majorly, retrospectively. Therefore, skin  
479 temperature could be a potentially useful parameter to be combined with other  
480 physiological measurements correlating with the onset of the fertile window and with  
481 ovulation for a more comprehensive modern fertility awareness method.

482

483

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487

488 **Competing Interests**

489 V.D.C., F.K., L.F., and B.M.G. are current or previous employees at Ava AG. B.L. is part  
490 of the Ava AG medical advisory board.

491

492 **Author Contribution**

493 B.L. conceived and designed the study. F.K., L.F., and M.S. conducted the study,  
494 collected, and processed the data. M.S. and B.M.G. analyzed the data. M.S., B.M.G.,  
495 V.C. and B.L. wrote the paper.

496

497 **Abbreviations**

498 BBT, basal body temperature; C, Celsius; LH, luteinizing hormone; LOESS, local  
499 regression smoothing; M, statistical mean; OV, ovulation day; S.D., standard  
500 deviation; WST, wrist skin temperature

501

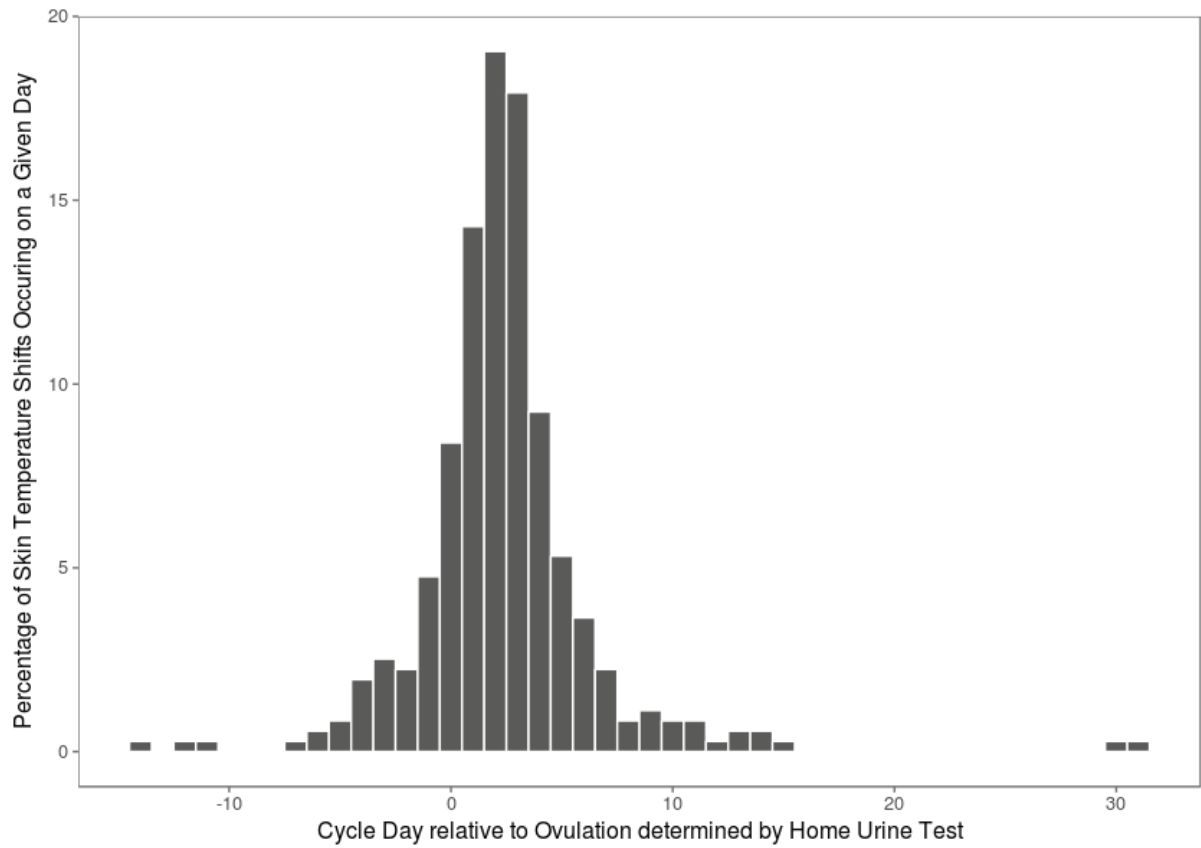
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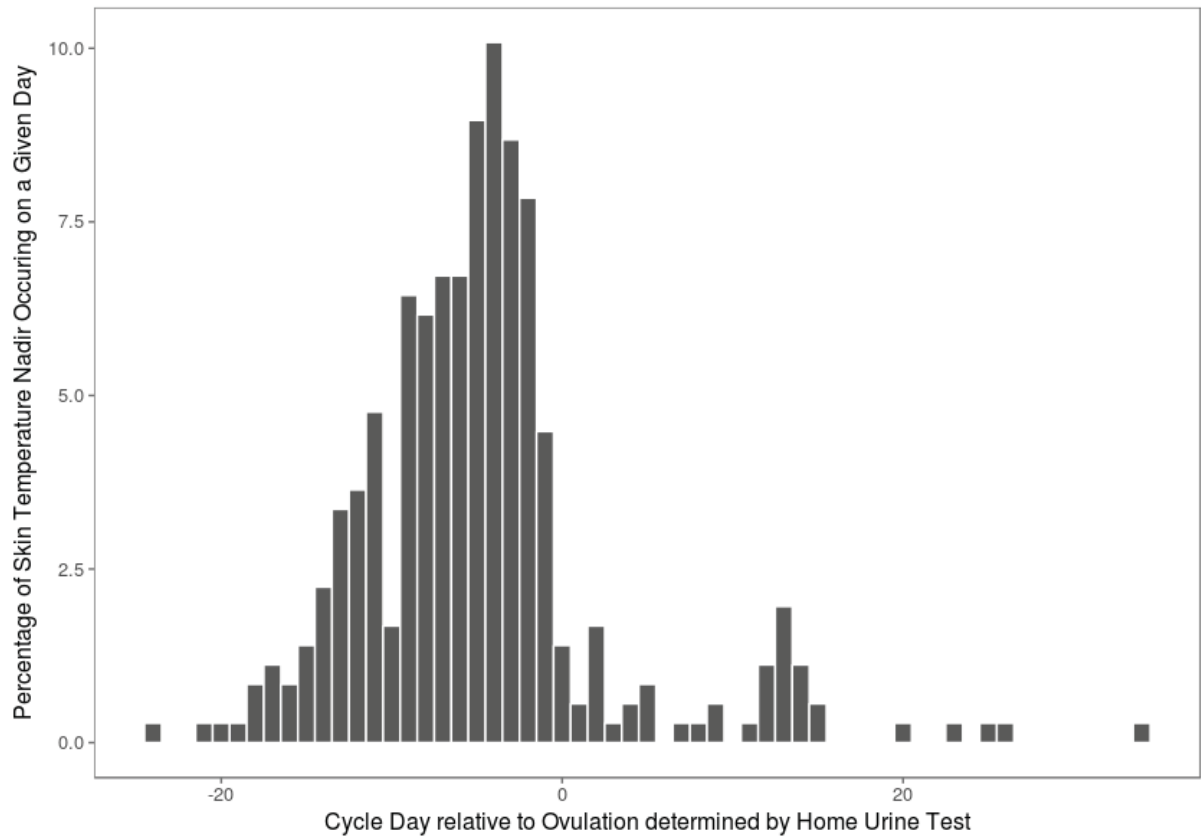


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663 **Figure 1. A histogram of the percentage of temperature shifts occurring on**  
 664 **a given day with reference to home LH test (n=307).**

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**Figure 2. A histogram of the percentage of days on which the lowest temperature was observed in a given cycle with reference to home LH test (n=307).**

670 **Tables**

671 *Table 1. Multi-level, linear mixed model of the relationship between menstrual phase and sleeping*  
672 *wrist-skin temperature*

673 *Table 2. Multi-level, linear mixed models of the relationship between menstrual phase, covariates, and sleeping*  
674 *wrist-skin temperature*

675 *Table 3. Multi-level, linear mixed model of the relationship between menstrual phase and sleeping*  
676 *wrist-skin temperature, controlling for all significant covariates*

TABLE 1. MULTI-LEVEL LINEAR MIXED MODEL OF THE RELATIONSHIP BETWEEN MENSTRUAL PHASE AND SLEEPING WRIST-SKIN TEMPERATURE

	Unstandardized B-coefficients	Standard error
INTERCEPT	35.06	0.10
CYCLE PHASE		
Menstrual	Reference	Reference
Follicular	-0.01	0.04
Fertile	-0.13***	0.02
Early-luteal	0.24***	0.02
Late-luteal	0.37***	0.03

Note: \*, \*\*, \*\*\* refer to  $P < 0.05$ , 0.01, 0.001 respectively

TABLE 2. MULTI-LEVEL, LINEAR MIXED MODELS OF THE RELATIONSHIP BETWEEN MENSTRUAL PHASE, COVARIATES, AND SLEEPING WRIST-SKIN TEMPERATURE

	MODEL 1	MODEL 2	MODEL 3	MODEL 4	MODEL 5	MODEL 6	MODEL 7	MODEL 8
Cycle phase								
Menstrual	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Follicular	-0.03 (0.03)	-0.01 (0.03)	-0.03 (0.03)	-0.02 (0.00)	-0.03 (0.03)	-0.03 (0.03)	-0.03 (0.03)	-0.03 (0.03)
Fertile	-0.13***(0.02)	-0.12***(0.01)	-0.13***(0.02)	-0.13***(0.00)	-0.12***(0.01)	-0.13***(0.02)	-0.13***(0.02)	-0.13***(0.02)
Early-luteal	0.24***(0.02)	0.24***(0.02)	0.24***(0.02)	0.24***(0.00)	0.24***(0.02)	0.24***(0.02)	0.24***(0.02)	0.23***(0.02)
Late-luteal	0.37***(0.03)	0.38***(0.03)	0.37***(0.03)	0.37***(0.00)	0.37***(0.01)	0.37***(0.03)	0.37***(0.03)	0.37***(0.03)
Meal <sup>a</sup>								
Small or no food	Reference							
Medium sized meal	-0.02 <sup>+</sup> (0.01)							
Large meal	-0.03**(0.01)							
Body Mass Index (kg/m <sup>2</sup> )		-0.05***(0.01)						
Coffee <sup>a</sup>								
No coffee			Reference					
≥ 1			-0.01 (0.01)					
Exercise <sup>a</sup>								
No exercise				Reference				
<60 minutes				0.01 (0.01)				
>60 minutes				0.02 (0.01)				
Sexual Intercourse <sup>a</sup>					-2.30*(0.01)			
Alcohol <sup>a</sup>								
No alcohol						Reference		
1-4 units						0.00 (0.01)		
≥5 units						0.06**(0.02)		
Age (years)							0.02 (0.01)	
Spotting								-0.01 (0.02)

Note: Unstandardized b-coefficient values reported, with standard errors in parentheses

a: Within the 3 hours preceding the onset of sleep; <sup>+</sup>, \*, \*\*, \*\*\* refer to  $P < 0.10, 0.05, 0.01, 0.001$  respectively

TABLE 3. MULTI-LEVEL, LINEAR MIXED MODEL OF THE RELATIONSHIP BETWEEN MENSTRUAL PHASE AND SLEEPING WRIST-SKIN TEMPERATURE, CONTROLLING FOR SIGNIFICANT COVARIATES

	Unstandardized B-coefficients	Standard error
INTERCEPT	36.29	0.34
CYCLE PHASE		
Menstrual	Reference	Reference
Follicular	-0.01	0.03
Fertile	-0.11***	0.01
Early-luteal	0.25***	0.02
Late-luteal	0.38***	0.03
MEAL <sup>a</sup>		
Small or No Food	Reference	Reference
Medium Sized	-0.02 <sup>+</sup>	0.01
Large Meal	-0.04***	0.01
BODY MASS INDEX (KG/M <sup>2</sup> )	-0.05***	0.01
SEXUAL INTERCOURSE <sup>a</sup>	-0.02*	0.01
ALCOHOL <sup>a</sup>		
No Alcohol	Reference	Reference
1-4 Units	0.01	0.01
≥5 Units	0.07***	0.02

a: Within the 3 hours preceding the onset of sleep

Note: <sup>+</sup>, \*, \*\*, \*\*\* refer to  $P < 0.10, 0.05, 0.01, 0.001$  respectively