

It's a bout time: cough bouts as a measure of severity

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Introduction

The most obvious application of a cough monitor – a device that timestamps individual coughs – is simply counting how many times a person coughs in a given period of time, typically one day. Dividing the resulting count by the overall monitoring time yields the person's cough rate, their average number of coughs per hour; daily cough rate has, to date, been the standard endpoint in cough studies and antitussive trials [1], [2].

Until recently, technological limitations forced this endpoint to be based on episodic 24-hour cough monitoring. Fortunately, this is no longer the case. Long-term, unobtrusive, and continuous cough monitoring technology makes open-ended cough monitoring feasible for the first time [3]. Instead of being limited to occasional estimates of a patient's cough rate, coughs can now be precisely timestamped day after day, for as long as desired, delivering holistic insights that were never available before. Already, longitudinal cough data have shown that 24-hour snapshots of coughing can produce unrepresentative cough rate estimates for people with volatile cough patterns, patterns that can only be identified through longitudinal monitoring [4].

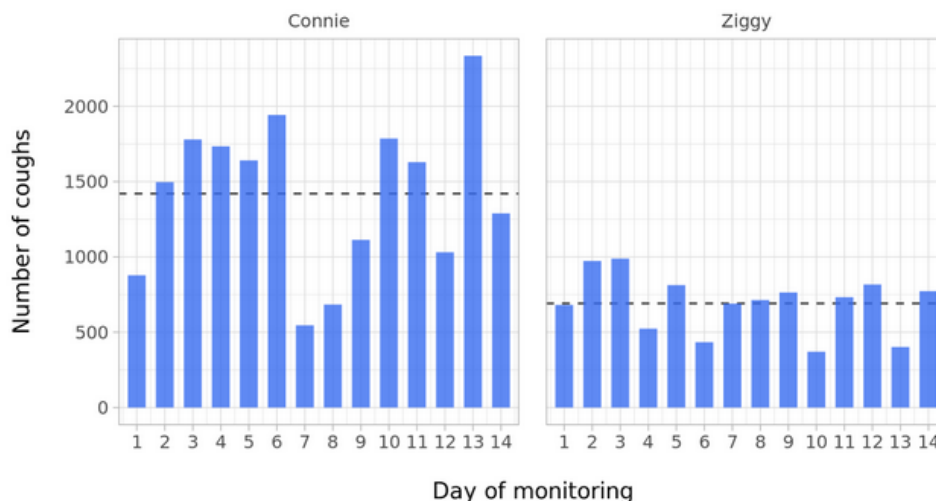
Continuous unobtrusive cough monitoring now enables an analysis of cough patterns and how they capture the lived experiences of coughers – how patients experience their cough, not just how many times they cough. Of particular importance are intense cough attacks, commonly called bouts, fits, epochs, and fits, that have profound influences on coughers [5].

To date researchers have used a variety of largely arbitrary definitions of bouts, mostly relying on a definition based on inter-cough intervals. Recently, Holt et al. published an important paper which used recordings that precisely timestamped coughs over 24 hours to determine which patterns of cough best correlated with the research subject's subjective experience of coughing as quantified by VAS scores [6]. They concluded that their analysis favored definitions of cough bouts utilizing inter-cough intervals of at most 3 seconds, despite not finding a statistically significant correlation between bouts defined as such and VAS scores. Interestingly, their supplementary data show that the sizes of intense periods of coughing – measured either by the number of coughs or the overall duration in time – were statistically correlated to VAS.

Here we delve further into cough bouts using data from two chronic coughers with two weeks of timestamped cough data. We demonstrate that the definition of a cough bout that has been used to date is arbitrary and ineffective at accurately describing the bout phenomenon. The following examples suggest, moreover, that simply varying the underlying parameters will not lead to an acceptable universal definition; bouts must be defined in coordination with the experiences of people with problematic cough. Thanks to the advent of continuous cough monitoring technology and the availability of uninterrupted longitudinal cough data, this important work is finally possible.

Cough counts are not enough

To see that a chronic cougher’s experience and quality of life cannot be inferred from cough counts alone [7], consider two weeks of cough data from two different chronic coughers, whom we’ll call Connie and Ziggy:



Each bar’s height is the number of coughs recorded on that day, and each dashed line indicates the cougher’s mean number of coughs per day over the two-week period (1,420 for Connie, 691 for Ziggy). It’s clear that Connie coughs far more than Ziggy on a daily basis, so one might reasonably conclude that coughing is more of a problem for Connie, perhaps causing increasing exhaustion over the course of the day. But not all coughs have equal impact – bouts leading to incontinence, breathlessness, emesis or embarrassment may have a profound negative impact on quality of life. Unfortunately, it is impossible to see the temporal structure of Connie’s or Ziggy’s coughs just by looking at these daily counts¹.

For anyone interested in cough, bouts are compelling and familiar – at an intuitive level, people immediately understand what a bout of coughing is. But what is a bout exactly? How should this concept be turned into a well-defined metric? Here is a common definition that has been around for years [8], [9], [10]:

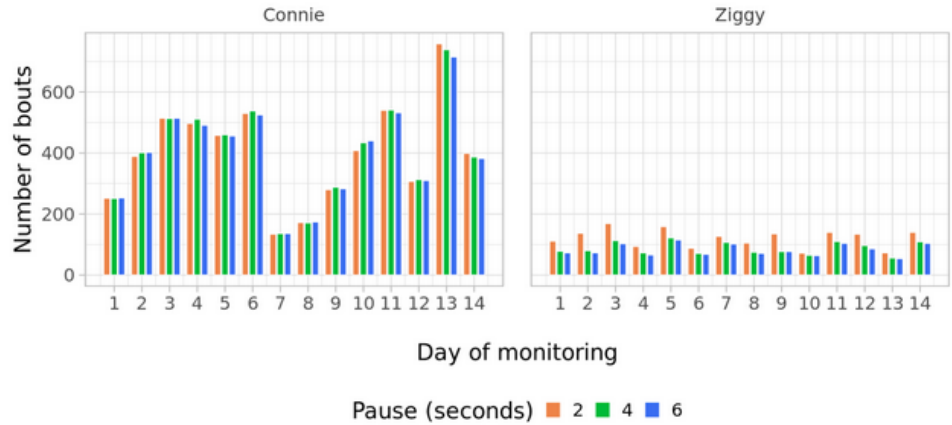
A bout is a series of 2 or more coughs without a pause of 2 seconds or longer between consecutive coughs.

While implementing this definition is straightforward, there has been no clear rationale for using a pause of 2 seconds or a minimum of 2 coughs. Why not use a shorter or longer pause? What if, to count as a meaningful bout, more than two coughs are required? With timestamps of individual coughs in hand, it is easy to explore what happens as these two parameters vary.

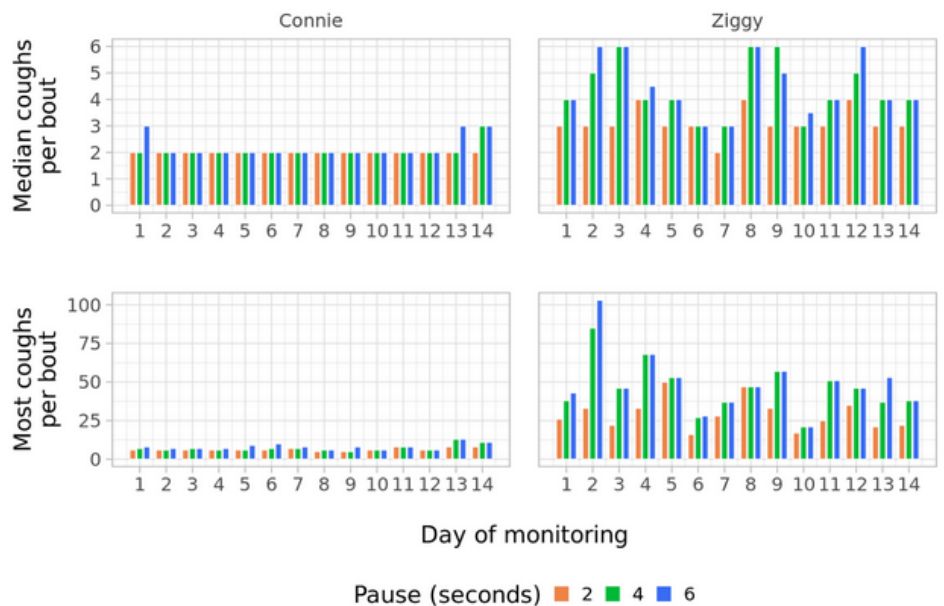
¹Other aspects of their coughing, such as severity, diurnal variation, and triggers, are equally invisible. While bouts are the focus of this paper, subsequent work will explore these other important dimensions. For all of these lines of research, progress requires moving beyond basic cough counting to secondary measures derived from the timestamps of continuously tracked individual coughs.

Pause between coughs

To investigate how bouts depend on the specified pause between consecutive coughs, suppose until further notice that a bout can contain as few as two coughs. For the two weeks of cough data summarized above, here are the daily numbers of cough bouts for Connie and Ziggy using three different pause lengths: 2 seconds (orange), 4 seconds (green), and 6 seconds (blue).

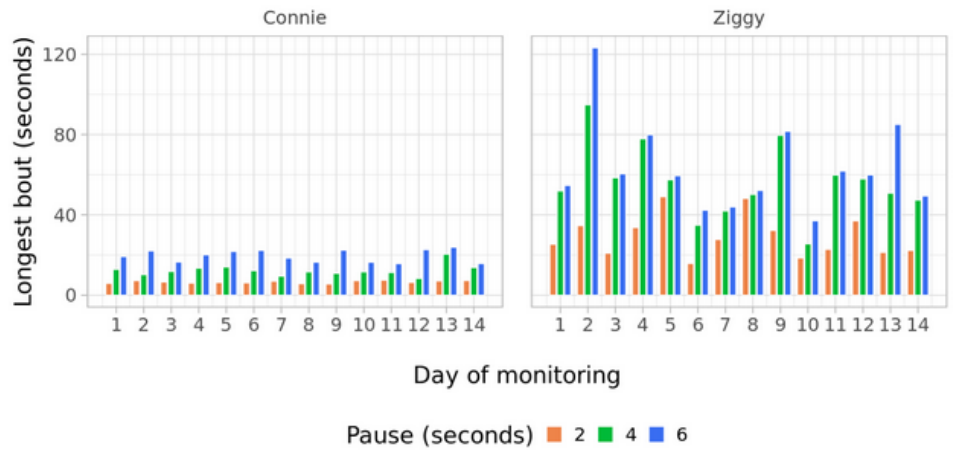


At first glance, it might still seem like coughing is a bigger problem for Connie than for Ziggy. But look closer: Connie's daily bout counts don't change much as the length of the pause changes, but Ziggy's daily bout counts tend to drop significantly when the pause increases past 2 seconds. To see what might be going on, let's look at how many coughs their bouts contain. Here are their daily median numbers of coughs per bout and their biggest bouts per day as measured by number of coughs:

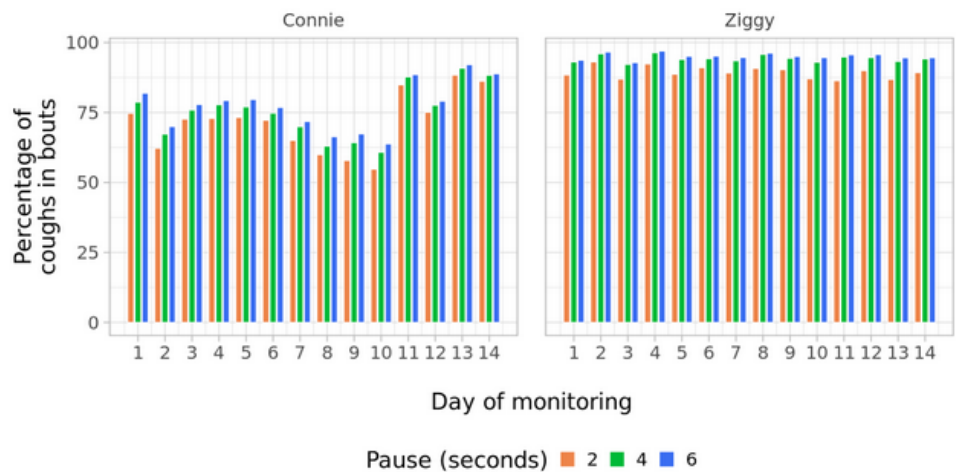


These two plots explain what's happening: Connie tends to cough twice – but no more – in rapid succession, while Ziggy tends to cough in waves that coalesce as the length of the allowed pause increases. There is further evidence of this in the durations

of their longest bouts per day:



Finally, it is interesting to compare the proportions of coughs contained in bouts from day to day. Almost all of Ziggy's coughs were contained in bouts, whereas 20% to 5% of Connie's coughs were isolated on most days:

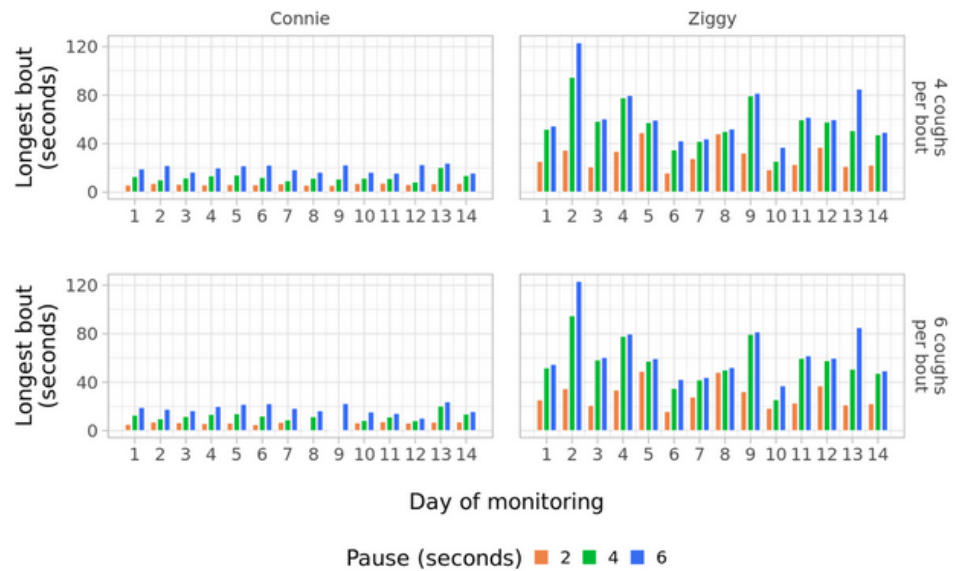
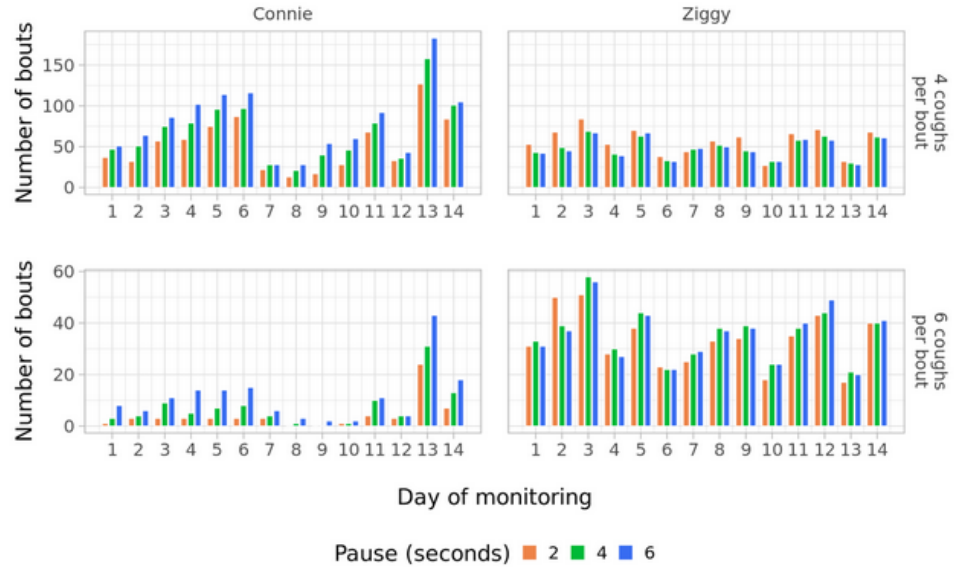


These results demonstrate some of the challenges of defining bouts: daily bout counts, bout durations, and numbers of coughs per bout will all vary, sometimes significantly, for different pause lengths. Simply comparing numbers of bouts seems particularly futile: Connie's double coughs translate into having far more bouts per day than Ziggy, but Ziggy's coughing episodes last much longer, contain more coughs, and likely produce a more profound negative impact on quality of life. Would this ambiguity be resolved if double coughs did not qualify as bouts?

Minimal number of coughs

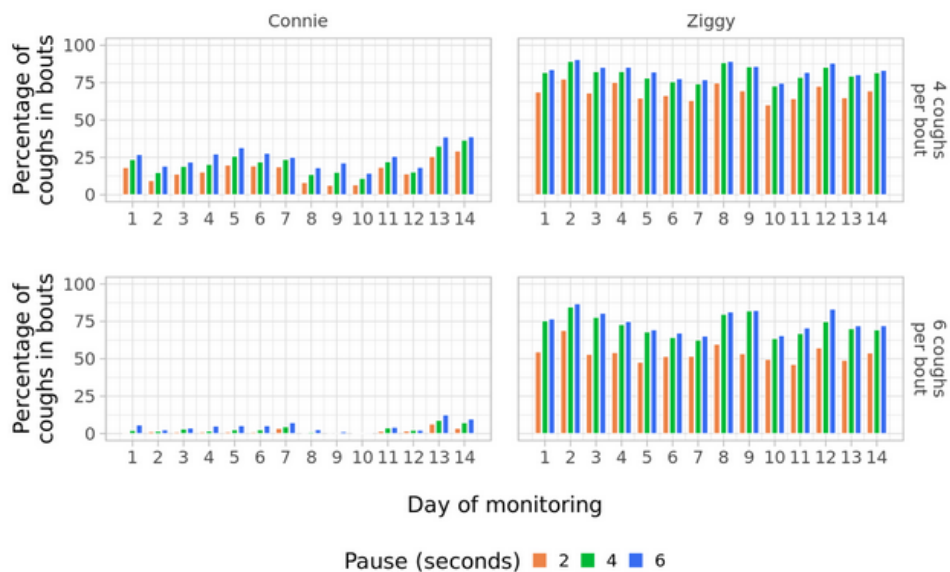
Just coughing twice within a few seconds is a radically different experience from coughing many times in a row over a minute or longer – classifying these two events with the same label obscures more than it reveals. To explore what happens as the minimal number of coughs per bout changes, consider requiring either 4 or 6 coughs per

bout. Here are the resulting numbers of bouts per day for Connie and Ziggy, along with their longest bouts per day:



As expected, the overall number of bouts decreases as the minimum number of required coughs increases. As might not have been expected from an initial inspection of daily cough counts, however, Connie's bouts reduce drastically when requiring 4 or 6 coughs. Ziggy continues to be plagued by bouts regardless, and the lengths of Ziggy's longest bouts are unaffected by changing either bout parameter. The same dramatic divergence is evident in the proportions of their coughs that are contained in bouts:

When a bout is defined as 4 or more coughs, Connie's coughs occur in bouts less than 25% of the time on most days; when a bout is defined as 6 or more coughs, Connie's coughs occur in bouts less than 10% of the time on all but two days. Ziggy's coughs, in contrast, are strikingly bout-intensive on every day, for every parameter setting.



Conclusions

Far from suggesting or attempting to justify a new definition of a cough bout, these examples show that changing the parameters that define a bout – the pause between coughs and the minimum number of coughs – yields very different results. Recent efforts suggesting that bout duration correlates with VAS suggest other definitions that potentially correspond better to cougher experience and to quality-of-life measures [6], [10]. Regardless of how bouts are defined, they should correlate with cough severity as actually experienced by individual coughers; there is no reason to believe that this is achieved by the conventional formulation with a 2-second pause and a 2-cough minimum. Similarly, though a 3-second pause does appear to correlate better with VAS, it is shown to do so in Holt et al. [6] using the 2-cough minimum, which we find questionable; the choice of a 2-cough minimum is likely well below what a person with a problematic chronic cough would define as a cluster of meaningful significance, an event connected to the psychological or physical harm caused by their coughing.

As with the 2-second, 2-cough concept, any attempt to define bouts universally with arbitrarily chosen parameters is unlikely to produce an acceptable metric of cough severity. Instead, clinical research and drug development trials should collect feedback from participants, ideally in real time, while continuously recording the timestamps of their coughs. This feedback should allow participants to identify the cough episodes that they consider most impactful, such as periods of coughing that cause fatigue, retching, or incontinence; a coordinated analysis of these events and their concomitant coughs would allow a rigorous approach to defining bouts that is grounded in patient experience.

References

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