Injury risk increases minimally over a large range of the acute:chronic workload ratio in children

Chinchin Wang\textsuperscript{1,2}, Tyrel Stokes\textsuperscript{3}, Jorge Trejo Vargas\textsuperscript{3}, Russell Steele\textsuperscript{3}, Niels Wedderkopp\textsuperscript{4}, Ian Shrier\textsuperscript{1}

\textsuperscript{1} Centre for Clinical Epidemiology, Lady Davis Institute, Jewish General Hospital, McGill University, 3755 Côte Ste-Catherine Road, Montreal, Quebec, Canada H3T 1E2

\textsuperscript{2} Department of Epidemiology, Biostatistics and Occupational Health, McGill University, 1020 Pine Avenue West, Montreal, Quebec, Canada H3A 1A2

\textsuperscript{3} Department of Mathematics and Statistics, McGill University, 805 Sherbrooke Street West, Montreal, Quebec, Canada H3A 0B9

\textsuperscript{4} Orthopedic Department University Hospital of South West Denmark, Department of Regional Health Research, University of Southern Denmark

**Corresponding Author:**

Ian Shrier MD, PhD

Centre for Clinical Epidemiology, Lady Davis Institute, Jewish General Hospital, McGill University, 3755 Côte Ste-Catherine Road, Montreal, Quebec, Canada H3T 1E2

Email: ian.shrier@mcgill.ca

Phone Number: 1-514-229-0114
ABSTRACT

**Background:** Limited research exists on the association between increased physical activity and injury in children.

**Objective:** To assess how well different variations of the acute:chronic workload ratio (ACWR) predict injury in children.

**Methods:** We conducted a prospective cohort study using data from 1670 Danish schoolchildren measured over 5.5 years. Coupled 4-week, uncoupled 4-week, and uncoupled 5-week ACWRs were calculated using activity frequency in the past week as the acute load and average weekly activity frequency in the past 4 or 5 weeks as the chronic load. We used new onset pain as a proxy for injury, and modelled its relationship with different ACWR variations using generalized linear and generalized additive models, with and without accounting for repeated measures.

**Results:** The relationship between the ACWR and injury risk was best represented using a generalized additive mixed model for the uncoupled 5-week ACWR. This model predicted an injury risk of ~3% when activity increased by up to 50% or decreased by up to 20% (0.8 ≤ ACWR ≤ 1.5). Larger decreases in activity were associated with a decreased injury risk to a minimum of 1.5%. Larger increases in activity were associated with an increased injury risk, from 3% up to a maximum of 6% at ACWR = 5. Girls were at significantly higher risk of injury than boys.

**Conclusion:** Increases in physical activity in children are associated with much lower increases in injury risk compared to previous results in adults.

**KEYWORDS**
Acute:chronic workload ratio, children, physical activity, injury risk, load
INTRODUCTION

Although physical activity is crucial for children’s development,\(^1\) increased activity is associated with increases in injury risk and related morbidities.\(^2\,3\) There are limited research and guidelines on the amount by which children can increase activity while minimizing injury.\(^4\)

The relationship between changes in activity and injury has been evaluated in adults using the acute:chronic workload ratio (ACWR).\(^5\) Although the ACWR cannot be used to determine the causal effect of increasing activity on injury, it is easy to interpret and may be useful for predicting injury when appropriately implemented.\(^6\)

There are many variations of ACWR. Traditionally, it is the activity in the past week (acute load) divided by an unweighted average of activity in the past 4 weeks (chronic load).\(^7\) This calculation is “coupled”, as the numerator is included in the denominator, and has conceptual limitations.\(^6\,8\) In the “uncoupled” variation, the numerator is excluded from the denominator.\(^9\) In exponentially weighted moving averages (EWMA) variations, activity performed further in the past is down-weighted.\(^10\) There is limited research regarding which variations best predict injury. An International Olympic Committee (IOC) consensus model identified coupled ACWRs between 0.8 and 1.3 as being associated with the lowest injury risk in adults, with increasing risk as ACWRs decrease below 0.8 and increase above 1.3.\(^11\) Despite being presented as a validated model, it suffers from limitations that threaten its utility even as a predictive tool.\(^6\) In addition, the ACWR-injury risk relationship has typically been modelled using generalized linear models (GLM; e.g. logistic regression).\(^12\,13\) GLMs restrict the type of relationship between the exposure (ACWR) and outcome (injury) to be the same over the entire range of exposure.\(^14\) Generalized additive models (GAM) are more flexible and might better model heterogenous relationships across the range.\(^14\)

Despite its limitations, the ACWR is currently one of few methods to predict the relationship between changes in activity and injury. Our objective is to apply different ACWR variations (coupled and uncoupled) and models (GLM and GAM without and with random effects) to predict the relationship between injury risk and changes in activity in children. As long as the results are interpreted as predictive and not causal, ACWR-based analyses can help with clinical
management predictions, and generate hypotheses that could later be tested with randomized trials or other appropriate methods that control for confounding.

METHODS

Data Source

This was a prospective cohort study nested within the Childhood Health, Activity, and Motor Performance School Study Denmark (CHAMPS-DK) that followed over 1000 schoolchildren for 5.5 years. A natural experiment occurred in Svendborg, Denmark where some schools increased physical education (PE) to six classes per week while others remained at two. CHAMPS-DK evaluated the health outcomes of the children in these different schools and has over 50 published papers. All children in the thirteen primary schools that agreed to participate were eligible for the study.

Our study uses physical activity and pain data collected via SMS messages from November 2008 to June 2014. Parents were asked each week whether their child experienced pain in different body locations in the past week, and whether pain was new or continuing from a previous injury. Parents were also asked for the number of times their child participated in leisure-time activity in the past week. This was added to the number of school activity sessions to get a total activity frequency for the week. Six PE classes were considered equivalent to three activity sessions and two PE classes were considered equivalent to one activity session to account for time spent changing and showering.

Participants could enter or leave the study at any time. We included all participants who provided SMS data. Data were collected throughout the school year (September to June). Missing data during school years were multiply imputed using resampling with matching with five datasets. Where ten or more weeks of data were missing in a row for an individual, these weeks were censored and excluded from analyses.

ACWR Variations

The exposure was one’s ACWR for the week, calculated as acute load divided by chronic load. For the coupled 4-week ACWR, acute load was the activity frequency in the index week (week of calculation) and chronic load was the average activity frequency across the index week and
previous 3 weeks (numerator included in denominator). For the uncoupled 4- and 5-week ACWRs, acute loads were the activity frequency in the index week and chronic loads were the average activity frequency in the previous 3 and 4 weeks respectively (numerator excluded from denominator).

Conventional EWMA variations of the ACWR use daily loads.\textsuperscript{10} We explored a modified EWMA where the acute load was the unweighted index week and chronic load was a weighted average of the previous 3 or 4 weekly loads. These models had much poorer fit than other ACWR variations (Supplemental Material 1) and were dropped from consideration.

**Outcome Definition**

The outcome was new onset pain, considered a proxy for new injury. New onset pain referred to new pain in any body location for the index week.

**Statistical Analyses**

The relationship between 3 variations of the ACWR (coupled 4-week; uncoupled 4-week; uncoupled 5-week) and injury (dichotomized to yes/no) was modelled using various regression approaches. For each variation, data were analyzed using GLMs and GAMs without random effects, and with a random intercept for individuals (mixed models; GLMM and GAMM). While we assessed the effect of including a random intercept for school, this effect was non-significant (p=0.5) and models were qualitatively very similar. The number of thin-plate spline basis functions was set to 7 for GAM and GAMMs. Each model used a logit link and treated the ACWR as an underlying continuous variable. The Akaike information criterion (AIC) was used to assess goodness of fit.\textsuperscript{17} A detailed description of model selection is provided in Supplemental Material 2.

Models were superimposed to compare ACWR variations and model types. To visualize the consequences of including random effects in GLMMs and GAMMs, we included observed probabilities of injury for each value of the uncoupled 4-week ACWR, discretized to the nearest 0.1. We included 95% confidence intervals (95% CI) accounting for random effects and histograms with the number of entries at each discretized ACWR value to illustrate uncertainty.

The uncoupled 5-week GAMM appeared to best model the relationship between the ACWR and injury risk based on AIC and model comparisons. Therefore, to assess the significance of gender,
fixed effects were included in separate GAMMs for the uncoupled 5-week ACWR and their p-value calculated. Sensitivity analyses were conducted excluding those who performed no activity during a given week (ACWR = 0) or those who did not change their activity over consecutive weeks (ACWR = 1) to assess their potential influence.

Based on the uncoupled 5-week GAMM results, we calculated the sample sizes required to detect a significant effect of doubling activity on injury risk using various randomized trial designs. Analyses were conducted in R 3.6.0, specifically the lme4\textsuperscript{18}, mgcv\textsuperscript{19}, and gamm4\textsuperscript{20} packages.

**Patient and Public Involvement**

Patients and the public were not involved in the design, conduct and dissemination of results of this study.

**RESULTS**

Out of 1755 children who participated in CHAMPS-DK, 1670 children aged 6 to 17 were included in our study and followed for an average of 3.8 years. This represented 286,536 weeks of data, of which 11,458 (4%) had injury. Children who provided SMS data were generally similar in age, gender and school type as those who did not (Table 1). Data on total household income and birthplace were mostly missing in non-participants. A participant flow diagram is shown in Supplemental Material 3.
Table 1. Baseline characteristics of participants included in study. Characteristics were measured at time of enrollment into the Childhood Health, Activity, and Motor Performance School Study Denmark. Participants were included if they provided data allowing at least one ACWR to be calculated.

| Characteristic                      | Total n=1741 | Included n=1660 | Excluded n=81 |
|-------------------------------------|--------------|-----------------|---------------|
| **Gender**                          |              |                 |               |
| Boy                                 | 803          | 769 (46%)       | 34 (42%)      |
| Girl                                | 874          | 846 (51%)       | 28 (35%)      |
| Unknown                             | 64           | 45 (3%)         | 19 (23%)      |
| **Grade (age)**                     |              |                 |               |
| 0-1 (6-9)                           | 673          | 644 (39%)       | 29 (36%)      |
| 2-3 (8-11)                          | 741          | 709 (43%)       | 32 (40%)      |
| 4 (10-12)                           | 327          | 307 (18%)       | 20 (25%)      |
| **School type**                     |              |                 |               |
| 3 PE sessions*/week                 | 995          | 955 (58%)       | 40 (51%)      |
| 1 PE sessions/week                  | 746          | 705 (42%)       | 41 (49%)      |
| **Total Household Income**          |              |                 |               |
| < kr 400,000                        | 179          | 178 (11%)       | 1 (1%)        |
| kr 400,000 to 599,000               | 351          | 351 (21%)       | 0 (0%)        |
| kr 600,000 to 799,000               | 345          | 344 (21%)       | 1 (1%)        |
| > kr 800,000                        | 184          | 184 (11%)       | 0 (0%)        |
| Unknown                             | 682          | 603 (36%)       | 79 (98%)      |
| **Birthplace**                      |              |                 |               |
| Denmark                             | 1290         | 1265 (76%)      | 25 (31%)      |
| Outside Denmark                     | 47           | 46 (3%)         | 1 (1%)        |
| Unknown                             | 404          | 349 (21%)       | 55 (68%)      |

* PE session: Physical education activity sessions where 2 physical education classes counted as 1 session to account for time spent changing and showering
Uncoupled vs. Coupled ACWR

Traditional GLMs for the uncoupled and coupled 4-week ACWRs are presented in Figure 1. The coupled and uncoupled 4-week ACWRs use the same data, but have different denominators. The coupled ACWR is constrained to \( \leq 4.9 \) In our data, the coupled ACWR reached a maximum of 3.5, whereas the uncoupled 4-week ACWR extended upwards to ACWR = 21.0 (Figure 1A). Whereas mean injury risk reached 8% for the coupled 4-week ACWR, risk extended to 62% for the uncoupled 4-week ACWR under GLMs (Figure 1B). We focus on the uncoupled ACWR for subsequent analyses because it is not constrained.

Uncoupled 4-week vs. 5-week ACWR

Table 2 illustrates AICs for all models. AICs for uncoupled 5-week models were lower than the uncoupled 4-week ACWR model, indicating that inclusion of the extra week in the uncoupled 5-week denominator improved model fit. Therefore, we focus on the uncoupled 5-week ACWR for remaining analyses.
Table 2. Akaike information criteria (AIC) for injury as a function of the acute:chronic workload ratio (ACWR) variation for generalized linear models (GLM), generalized linear mixed models (GLMM), generalized additive models (GAM), and generalized additive mixed models (GAMM).

|                  | Coupled 4-week | Uncoupled 4-week | Uncoupled 5-week |
|------------------|----------------|------------------|------------------|
| **Generalized linear model** |                |                  |                  |
| GLM (No random effect) | 83,709         | 83,759           | 80,931           |
| GLMM (Random effect)   | 80,650         | 80,701           | 77,956           |
| **Generalized additive model** |                |                  |                  |
| GAM (No random effect) | 83,492         | 83,714           | 80,892           |
| GAMM (Random effect)   | 80,498         | 80,681           | 77,927           |
Incorporating Random Effects (Mixed Models)

GLMMs and GAMMs account for repeated measures by including a random intercept for individuals. Compared to models without random effects (GLMs and GAMs), they had consistently better fit across all ACWR variations (Table 2), and predicted a lower injury risk across the uncoupled 5-week ACWR range (Figure 2A and 2B). These results are consistent with the general belief that individuals with different characteristics have different baseline probabilities of getting injured. We focus on mixed models for the uncoupled 5-week ACWR for remaining analyses.

Generalized Linear vs. Additive Mixed Models

GLMMs assume that the function describing the relationship between exposure (ACWR) and outcome (injury) is constant across the range of exposure. In contrast, GAMMs allow for multiple functions across the ACWR range. Figure 2A and 2B display the GLMM and GAMM for the uncoupled 5-week ACWR, with a limited range for clarity (full range shown in Supplemental Material 4). In our data, the GLMM predicted exponential increases in risk throughout the ACWR range. When activity was unchanged (ACWR = 1), injury risk was 3%. When activity decreased (ACWR < 1), the GLMM predicted a gradual decrease in risk to 2% at ACWR = 0 (relative risk compared to ACWR = 1; RR_{ACWR=1} = 0.7). When activity increased (ACWR > 1), the GLMM predicted an increase in risk to 8% at ACWR = 6 (RR_{ACWR=1} = 2.7) and to 24% at the maximum ACWR of 9.3.

In contrast, the GAMM predicted heterogenous relationships across the ACWR range (Figure 2B). There were minimal changes in risk as ACWR decreased from 1 to 0.8, followed by a gradual decrease in risk down to 1.5% at ACWR = 0 (RR_{ACWR=1} = 0.5). Minimal changes in risk were predicted with increases in ACWR from 1 to 1.5. As the ACWR increased further, there was a gradual increase in risk up to a maximum of 6% at ACWR = 5 (RR_{ACWR=1} = 2.2), with large uncertainty at higher ACWRs. Because there were very little data above ACWR > 3 (Figure 2A and B; histograms), confidence intervals should be very wide at high ACWRs. While this was apparent in the GAMMs (Supplemental Material 4), the GLMMs had narrower and potentially unrealistic confidence intervals over the same range.
Because GAMMs had lower AICs than GLMMs, better modeled heterogenous relationships, and appeared to have more realistic confidence intervals, we focus on the uncoupled 5-week GAMM for subsequent comparisons.

**Stratification by Gender**

Uncoupled 5-week GAMMs stratified by gender suggested similar relationships between boys and girls at low ACWRs, but that girls may have a higher injury risk than boys at ACWR > 2 (Figure 3). There was a statistically significant association of gender when included in the overall GAMM (p = 0.047).

**Sensitivity Analyses**

We examined two potentially influential points in our data. First, 2% of data were from weeks where no activity was performed (ACWR = 0). Although these points were at the extreme of the x-axis with low uncertainty and might have had high leverage, the overall relationship after exclusion was qualitatively similar (Supplemental Material 5). Second, 30% of data were from weeks where activity was unchanged from the previous 4 weeks (ACWR = 1). GAMMs for the uncoupled 5-week ACWR including and excluding these weeks were also similar in shape (Supplemental Material 5).

**Sample sizes for randomized trials**

Based on our results, a simple randomized trial examining the effects of doubling activity on injury risk in children (risk = 3% at ACWR = 1 versus risk = 4% at ACWR = 2) would require 11,000 participants (5,500 per group). A repeated cross-over trial with weekly follow-up over 2 years without a washout period for cross-over effects (a typically unreasonable assumption) would require 665 participants (calculations in Supplemental Material 6).

**DISCUSSION**

The relationship between the ACWR and injury risk in our data was best represented by the GAMM for the uncoupled 5-week ACWR. Risk remained relatively stable at 3% when activity increased by up to 50% or decreased by up to 20% (0.8 ≤ ACWR ≤ 1.5). Further decreases in activity were associated with a decreased injury risk to a minimum of 1.5% at ACWR = 0. Larger increases in activity were associated with an increased injury risk to a maximum of 6%
(2-fold increased risk) at ACWR = 5 (5-fold increase in activity). There was a statistically significant effect of gender in this relationship, with girls at higher risk of injury at ACWR > 1 than boys.

**Differences between ACWR Variations**

Our study found differences between the uncoupled and coupled ACWR, with models increasingly diverging at coupled ACWR > 2. Although Gabbett et al. previously found no significant difference in injury risk between the coupled and uncoupled ACWR, their analyses were based on discretized ACWRs, with ACWRs greater than 2 analyzed as ACWR = 2.\(^{21}\)

However, uncoupled and coupled ACWRs only diverge at coupled ACWR > 1.5, with greater divergence at ACWR > 2 (Figure 1A). Pooling points at ACWR > 2 in Gabbett et al. likely obscured differences between the uncoupled and coupled ACWR at high ACWRs.

The uncoupled ACWR also has a simpler calculation and interpretation than the coupled ACWR. For the 4-week ACWR, it corresponds directly to the relative increase in activity compared to the previous 3 weeks. Conversely, the coupled ACWR is a proportion of current activity relative to activity in the current and previous 3 weeks. Therefore, we prefer the uncoupled ACWR.

Inclusion of an additional week in the uncoupled ACWR calculation improved model fit, suggesting that activity that occurred 5 weeks previous was associated with injury in our study context. We emphasize that causal interpretations would require different models and assumptions.

**Linear vs. Additive Models and Random Effects**

Previous studies typically modelled the ACWR-injury risk relationship using logistic regression (i.e. GLM),\(^{12,13}\) sometimes with quadratic terms.\(^{7,22-25}\) Like our study, some used mixed models (i.e. GLMM),\(^{22,23,26,27}\) to account for repeated measures, or generalized estimating equations\(^{28,29}\). Many studies did not account for repeated measures.\(^{7,12,13,24}\)

This is the first study to systematically explore these different models on the same data. In our data on children, mixed models predicted lower injury risks across the ACWR range (Figure 2). These differences demonstrate the importance of accounting for repeated measures to obtain population estimates.
This is also the first study to use GAMMs to model the ACWR-injury risk relationship. GAMMs were able to model heterogenous relationships in the data, including a stable injury risk around ACWR = 1 (Figure 2). GLMMs enforce a single functional form, which is unlikely to be true, and predicted exponential increases across the ACWR range. GAMMs also better accounted for uncertainty at high ACWRs where there were few data. While including polynomial (e.g. quadratic) terms would provide added flexibility over simple log-linear logistic regression, specifying the appropriate polynomial terms may not be straightforward. For example, the IOC consensus model used a quadratic function that suggested increasing risk below ACWR = 0.8, even though there is no biological explanation for this relationship. Therefore, we believe that GAMMs better predict the ACWR-injury risk relationship.

Comparison to IOC Consensus Model

Both our uncoupled 5-week ACWR GAMM in children and the coupled 4-week ACWR IOC consensus model in adults predicted minimal changes in injury risk when activity increased or decreased by 30%. However, the IOC consensus model predicted rapidly increasing risk beyond a coupled ACWR of 1.5 (uncoupled ACWR = 1.8), whereas the increase in our model was more gradual and only doubled despite a quintupling of activity (Figure 2B).

Additionally, unlike the IOC consensus model that suggested increases in injury risk when activity decreased by more than 50%, our model suggested continuing decreases in risk. This decrease was still present, albeit smaller, when we excluded data where ACWR = 0. The results from the IOC consensus model might be due to inappropriately grouping the continuous ACWR into categories prior to analysis, an artifact from using a quadratic function, or attributable to differences in study design (e.g. adults vs children).

Limitations

Despite a very large sample, we observed very few weeks at high ACWRs. We calculated ACWRs using 4 or 5 weeks of data, as per previous literature. More research is required to identify the most relevant time windows. Additionally, our load definition encompassed activity of different types and duration. A definition with less variation might increase precision, and our findings may not be generalizable to specific sporting contexts. Finally, the ACWR has serious limitations for assessing causality. More advanced methods that account for time-
dependent confounding need to be developed to evaluate the causal effect of changes in activity on injury risk in children.

**CONCLUSION**

The relationship between the ACWR and injury risk in children was best predicted using a GAMM for the uncoupled 5-week ACWR. Injury risk remained around 3% when activity was increased by up to 50% or decreased by up to 20% (0.8 \leq ACWR \leq 1.5). Injury risk decreased when activity was decreased by more than 20% (ACWR < 0.8) to a minimum of 1.5% at ACWR = 0, unlike previous studies in adults. Injury risk increased when activity increased by more than 50% (ACWR > 1.5) to a maximum of 6% at ACWR = 5, considerably less than reported in adult studies using less flexible methods. Although the ACWR has important limitations, we recommend that when implemented, researchers and practitioners use the uncoupled measure, account for repeated measures, and move beyond logistic models.
REFERENCES

1 Janssen I, LeBlanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. *Int J Behav Nutr Phys Act* 2010;7:40. doi:10.1186/1479-5868-7-40

2 Nauta J, Martin-Diener E, Martin BW, *et al.* Injury Risk During Different Physical Activity Behaviours in Children: A Systematic Review with Bias Assessment. *Sports Med* 2015;45:327–36. doi:10.1007/s40279-014-0289-0

3 Caine D, Caine C, Maffulli N. Incidence and distribution of pediatric sport-related injuries. *Clin J Sport Med* 2006;16:500–13. doi:10.1097/01.jsm.0000251181.36582.a0

4 Parrish A-M, Tremblay MS, Carson S, *et al.* Comparing and assessing physical activity guidelines for children and adolescents: a systematic literature review and analysis. *Int J Behav Nutr Phys Act* 2020;17:16. doi:10.1186/s12966-020-0914-2

5 Griffin A, Kenny IC, Comyns TM, *et al.* The Association Between the Acute:Chronic Workload Ratio and Injury and its Application in Team Sports: A Systematic Review. *Sports Med Auckl NZ* 2020;50:561–80. doi:10.1007/s40279-019-01218-2

6 Wang C, Vargas JT, Stokes T, *et al.* Analyzing Activity and Injury: Lessons Learned from the Acute:Chronic Workload Ratio. *Sports Med* 2020;50:1243–54. doi:10.1007/s40279-020-01280-1

7 Hulin BT, Gabbett TJ, Lawson DW, *et al.* The acute:chronic workload ratio predicts injury: high chronic workload may decrease injury risk in elite rugby league players. *Br J Sports Med* 2016;50:231–6. doi:10.1136/bjsports-2015-094817

8 Lolli L, Batterham AM, Hawkins R, *et al.* Mathematical coupling causes spurious correlation within the conventional acute-to-chronic workload ratio calculations. *Br J Sports Med* 2017;;bjsports-2017-098110. doi:10.1136/bjsports-2017-098110

9 Windt J, Gabbett TJ. Is it all for naught? What does mathematical coupling mean for acute:chronic workload ratios? *Br J Sports Med* 2018;;bjsports-2017-098925. doi:10.1136/bjsports-2017-098925

10 Williams S, West S, Cross MJ, *et al.* Better way to determine the acute:chronic workload ratio? *Br J Sports Med* 2017;51:209–10. doi:10.1136/bjsports-2016-096589

11 Soligard T, Schwellnus M, Alonso J-M, *et al.* How much is too much? (Part 1) International Olympic Committee consensus statement on load in sport and risk of injury. *Br J Sports Med* 2016;50:1030–41. doi:10.1136/bjsports-2016-096581

12 Malone S, Owen A, Newton M, *et al.* The acute:chronic workload ratio in relation to injury risk in professional soccer. *J Sci Med Sport* 2017;20:561–5. doi:10.1016/j.jsams.2016.10.014
13 Hulin BT, Gabbett TJ, Blanch P, et al. Spikes in acute workload are associated with increased injury risk in elite cricket fast bowlers. Br J Sports Med 2014;48:708–12. doi:10.1136/bjsports-2013-092524

14 Hastie T, Tibshirani R. Generalized additive models for medical research. Stat Methods Med Res 1995;4:187–96. doi:10.1177/096228029500400302

15 Wedderkopp N, Jespersen E, Franz C, et al. Study protocol. The Childhood Health, Activity, and Motor Performance School Study Denmark (The CHAMPS-study DK). BMC Pediatr 2012;12:128. doi:10.1186/1471-2431-12-128

16 Wang C, Stokes T, Steele R, et al. A logic-based resampling with matching approach to multiple imputation of missing data. ArXiv200406630 Stat Published Online First: 14 April 2020.http://arxiv.org/abs/2004.06630 (accessed 16 Apr 2020).

17 Akaike H. Information Theory and an Extension of the Maximum Likelihood Principle. In: Parzen E, Tanabe K, Kitagawa G, eds. Selected Papers of Hirotugu Akaike. New York, NY: Springer 1998. 199–213. doi:10.1007/978-1-4612-1694-0_15

18 Bates D, Maechler M, Bolker [aut B, et al. lme4: Linear Mixed-Effects Models using ‘Eigen’ and S4. 2020. https://CRAN.R-project.org/package=lme4 (accessed 29 Sep 2020).

19 Wood S. mgcv: Mixed GAM Computation Vehicle with Automatic Smoothness Estimation. 2020. https://CRAN.R-project.org/package=mgcv (accessed 29 Sep 2020).

20 Wood S, Scheipl F. gamm4: Generalized Additive Mixed Models using ‘mgcv’ and ‘lme4’. 2020. https://CRAN.R-project.org/package=gamm4 (accessed 29 Sep 2020).

21 Gabbett TJ, Hulin B, Blanch P, et al. To Couple or not to Couple? For Acute:Chronic Workload Ratios and Injury Risk, Does it Really Matter? Int J Sports Med 2019;40:597–600. doi:10.1055/a-0955-5589

22 Sampson JA, Murray A, Williams S, et al. Injury risk-workload associations in NCAA American college football. J Sci Med Sport 2018;21:1215–20. doi:10.1016/j.jsams.2018.05.019

23 Weiss KJ, Allen SV, McGuigan MR, et al. The Relationship Between Training Load and Injury in Men’s Professional Basketball. Int J Sports Physiol Perform 2017;12:1238–42. doi:10.1123/ijsppp.2016-0726

24 Blanch P, Gabbett TJ. Has the athlete trained enough to return to play safely? The acute:chronic workload ratio permits clinicians to quantify a player’s risk of subsequent injury. Br J Sports Med 2016;50:471–5. doi:10.1136/bjsports-2015-095445

25 Carey DL, Blanch P, Ong K-L, et al. Training loads and injury risk in Australian football—differing acute: chronic workload ratios influence match injury risk. Br J Sports Med 2017;51:1215–20. doi:10.1136/bjsports-2016-096309
26 Warren A, Williams S, McCaig S, et al. High acute:chronic workloads are associated with injury in England & Wales Cricket Board Development Programme fast bowlers. *J Sci Med Sport* 2018;21:40–5. doi:10.1016/j.jsams.2017.07.009

27 Ahmun R, McCaig S, Tallent J, et al. Association of Daily Workload, Wellness, and Injury and Illness During Tours in International Cricketers. *Int J Sports Physiol Perform* 2020;14:369–77. doi:10.1123/ijspp.2018-0315

28 Jaspers A, Kuyvenhoven JP, Staes F, et al. Examination of the external and internal load indicators’ association with overuse injuries in professional soccer players. *J Sci Med Sport* 2018;21:579–85. doi:10.1016/j.jsams.2017.10.005

29 McCall A, Dupont G, Ekstrand J. Internal workload and non-contact injury: a one-season study of five teams from the UEFA Elite Club Injury Study. *Br J Sports Med* 2018;52:1517–22. doi:10.1136/bjsports-2017-098473

30 Harrell FE. General Aspects of Fitting Regression Models. In: Harrell Jr Frank E, ed. *Regression Modeling Strategies: With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis*. Cham: Springer International Publishing 2015. 13–44. doi:10.1007/978-3-319-19425-7_2

31 Bolker B. *Ecological Models and Data in R*. Princeton University Press 2008.
CONTRIBUTORS
CW and IS were responsible for this study’s concept and design. NW was responsible for the concept and design of the parent study, and data collection. CW was responsible for data analysis, with assistance from TS, JTV, RS, and IS. CW and IS drafted the manuscript. All authors were involved in revising the manuscript.

COMPETING INTERESTS
None declared.

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ETHICS APPROVAL
All participation in the data collection was voluntary with the option to withdraw at any time. The study was approved by the Ethics Committee for the region of Southern Denmark (ID S20080047)

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**DATA SHARING**

Data are available upon reasonable request.
FIGURES

Figure 1. Comparison of the coupled and uncoupled 4-week acute:chronic workload ratio (ACWR) and their relationship with injury in children. A. Relationship between the coupled and uncoupled ACWR. The points correspond to observed values and the dashed line represents the theoretical maximum value of 4 for the coupled ACWR. B. Generalized linear models (logistic regression; no random effect) for the relationship between the coupled and uncoupled ACWR and injury. Lines represent models with 95% CI in shaded areas.
Figure 2. The relationship between the uncoupled 5-week acute:chronic workload ratio (ACWR) and injury in children, without a random effect and with a random effect (mixed model) for individuals. A. Generalized linear model (GLM) and generalized linear mixed model (GLMM). B. Generalized additive model (GAM) and generalized additive mixed model (GAMM). Lines represent models with 95% CI in shaded areas. Points represent observed probability of injury with 95% CI at ACWRs discretized to 0.1. As the point estimates do not account for repeated measures, the GLM and GAM follow the observed points (which also do not account for repeated measures) more closely than the GLMM and GAMM. Histograms show the number of entries at each discretized ACWR. The ACWR range (x-axis) is restricted to ≤ 6 for clarity.
Figure 3. The relationship between the uncoupled 5-week acute:chronic workload ratio (ACWR) and injury in children using generalized additive mixed models with a random effect for individuals; stratified by gender. Lines represent models with 95% CI in shaded areas. Horizontal dashed line represents pooled risk of injury at ACWR = 1, with relative risk versus ACWR = 1 shown on right y-axis. Histogram shows the number of entries at discretized ACWRs by gender. The ACWR range (x-axis) is restricted to ≤ 6 for clarity.
Table S1. Akaike information criteria (AIC) for injury as a function of exponentially weighted moving average (EWMA) acute:chronic workload ratio (ACWR) variations for generalized linear models (GLM), generalized linear mixed models (GLMM), generalized additive models (GAM), and generalized additive mixed models (GAMM). AICs for non-EWMA models were lower (better fit) and ranged from 77,000 to 84,000 (Table 2).

| EWMA ACWR Variation | Coupled 4-week | Uncoupled 4-week | Uncoupled 5-week |
|---------------------|----------------|------------------|------------------|
| Generalized linear model |                |                  |                  |
| GLM (No random effect) | 96,016         | 90,724           | 90,688           |
| GLMM (Random effect)   | 92,422          | 87,441           | 87,404           |
| Generalized additive model |                |                  |                  |
| GAM (No random effect)  | 95,840          | 90,457           | 90,438           |
| GAMM (Random effect)   | 92,310          | 87,277           | 87,255           |
SUPPLEMENTAL MATERIAL 2

The default maximum number of basis functions for GAMs and GAMMs using the mgcv\textsuperscript{1} and gamm4\textsuperscript{2} R packages is 9. Both R packages then adjust the number of basis functions based on an estimated smoothness parameter. While the estimated smoothness parameter for the GAMs and GAMMs for the uncoupled 5-week and coupled 4-week ACWRs suggested 9 basis functions to model the data, the estimated smoothness parameter for the GAMs and GAMMs for the uncoupled 4-week ACWR suggested 7 basis functions to model the data.

To compare ACWR variations, we set the number of basis functions to be fixed to 7 for all models. Although the uncoupled 5-week GAMM with default 9 basis functions had slightly better fit than the GAMM with 7 basis functions (77,850 vs. 77,927) when averaged over five imputed data sets, this was less than the difference observed between imputed datasets (minimum 77,832; maximum 78,332). The models for each of the 5 imputed datasets is shown in Figure S1. The GAMM with 9 basis functions also appeared to have considerable noise (Figure S2). Therefore, we considered the simpler model with 7 basis functions more appropriate for our analyses.
Figure S1. Generalized additive mixed models (GAMM) for the relationship between the uncoupled 5-week acute:chronic workload ratio and injury in children in different imputed datasets. Lines represent models with 95% CI in shaded areas. Akaike Information Criteria for each of the models varied between 77,832 to 78,332.
Figure S2. Comparison of generalized additive mixed models (GAMM) for the relationship between the uncoupled 5-week acute:chronic workload ratio and injury in children with 7 basis functions (b.f.) and 9 basis functions. Lines represent models with 95% CI in shaded areas. Points represent observed probability of new onset injury with 95% CI at ACWRs discretized to 0.1.
References:

1 Wood S. *mgcv: Mixed GAM Computation Vehicle with Automatic Smoothness Estimation*. 2020. https://CRAN.R-project.org/package=mgcv (accessed 29 Sep 2020).

2 Wood S, Scheipl F. *gamm4: Generalized Additive Mixed Models using “mgcv” and “lme4.”* 2020. https://CRAN.R-project.org/package=gamm4 (accessed 25 Apr 2020).
Figure S1. Participant flow diagram for study inclusion. Fourteen individuals were excluded as their ID numbers could not be linked to other study data. Eighty one individuals were excluded because they either did not provide SMS data, or had insufficient data to calculate acute:chronic workload ratios (ACWRs).
Figure S1. Generalized linear mixed models (GLMM) and generalized additive mixed models (GAMM) for the relationship between variations of the acute:chronic workload ratio (ACWR) and injury in children. A. Uncoupled 5-week ACWR. B. Uncoupled 4-week ACWR. C. Coupled 4-week ACWR. Lines represent models with 95% CI in shaded areas. The full ACWR range (x-axis) is shown for the uncoupled 5-week (maximum 9.3) and coupled 4-week ACWR (maximum 3.4); the range is restricted to ≤ 9.3 for the uncoupled 4-week ACWR for clarity and comparison to the uncoupled 5-week model.
Figure S1. Effect of excluding weeks with no activity or no change in activity on the relationship between the uncoupled 5-week acute:chronic workload ratio (ACWR) and injury in children using generalized additive mixed models with a random effect for individuals. A. Including ACWR = 0 (no activity performed in index week) and ACWR = 1 (no change in activity from previous weeks). B. Excluding ACWR = 0. C. Excluding ACWR = 1. Lines represent models with 95% CI in shaded areas. Points represent observed probability of new onset injury with 95% CI at ACWRs discretized to 0.1. Horizontal dashed line represents risk of injury at ACWR = 1, with relative risk versus ACWR = 1 on right y-axis. Histograms show the number of entries at each discretized ACWR. The ACWR range (x-axis) is restricted to ≤ 6 for clarity.
**Simple Randomized Trial (5 weeks total)**

To estimate the sample size for a simple randomized trial that included 4 weeks of the same amount of activity followed by 50% of the participants performing one additional week where 1) ACWR = 1 (no change in activity) or 2) ACWR = 2 (doubling activity), we used the following numbers:

- alpha = 0.05
- power = 0.8
- injury risk = 3% at ACWR = 1
- injury risk = 4% at ACWR = 2

The calculated sample size is 5,500 per group, or 11,000 participants total. Calculations were performed using PS: Power and Sample Size Calculation.¹

**Crossover Trial (1 crossover; 10 weeks total)**

It is possible to also conduct a crossover trial where individuals switch from ACWR = 1 to ACWR = 2, or vice versa. Both interventions in the simple randomized trial above require 5 weeks, with the only difference between them being the activity performed in the last week. For a cross-over trial, for simplicity, we will make the unrealistic assumption that there is no carry-over effect (no need for a washout period after the fifth week where activity either remains unchanged or is doubled).

Let us consider that each participant will perform only one cycle at ACWR = 1 and one cycle at ACWR = 2. Using a correlation between outcomes of 0.17 (as was seen in our data), we would require 2,055 participants. Calculations were performed using PS: Power and Sample Size Calculation.¹

**Crossover Trial (20 crossovers; 2 years total)**

The required sample size for a crossover trial where each participant performed each intervention many times can be estimated using a method typically used for cluster randomized trials.² In this
study, a cluster is defined by the repeated cycles of intervention for each participant. Since each intervention is 5 weeks long, we would need to follow participants for almost 2 years to obtain 10 cycles under each condition (cluster size = 20).

The required sample size for the cross-over trial is equal to the sample size for the simple RCT divided by an “inflation factor”. The inflation factor is dependent on the intra-class correlation (ICC) within a cluster. In our data, the ICC was 0.11 when restricted to participants with ACWR = 1 or ACWR = 2.

The inflation factor is calculated as:

$$1 + (n - 1) \times ICC,$$

where n is the size of the cluster (40 in this hypothetical study). Therefore,

$$Inflation \ factor = 1 + (20 - 1) \times 0.11 = 3.09.$$

The required sample size for a cross-over trial with 20 measures per cluster is:

$$\frac{Sample \ size \ not \ including \ Design \ Effect}{Inflation \ Factor} = \frac{2055}{3.09} = 665$$

Therefore, even if we assumed no washout period was necessary and other unlikely assumptions (e.g. no effect of injury on future risk of injury), we would need to follow 665 participants over 2 years to observe a 33% increase in risk (from 3% to 4%).
References:

1 Dupont WD, Plummer WD. Power and sample size calculations: A review and computer program. *Control Clin Trials* 1990;11:116–28. doi:10.1016/0197-2456(90)90005-M

2 Emery CA. Considering Cluster Analysis in Sport Medicine and Injury Prevention Research. *Clin J Sport Med* 2007;17:211–214. doi:10.1097/JSM.0b013e3180592a58