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An interactive tool to personalise 24-hour activity, sitting and sleep prescription for optimal health outcomes

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Title Page

Title: An interactive tool to personalise 24-hour activity, sitting and sleep prescription for optimal health outcomes.

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Abstract

Personalised interventions which optimise the balance of physical activity (PA), sleep and sedentary behaviour (i.e., time use) in the 24-hr day may be more effective than one-size-fits-all approaches. We present an interactive app to personalise 24-hr time use based on individuals' health and sociodemographic characteristics. Analyses used cross-sectional data from 53,057 UK Biobank participants. Average daily time use was measured using 7-day accelerometry data and expressed as a 24-hr composition using isometric log-ratio transformation. Five cognitive composites were derived from web-based tests. Regularized linear regression examined the relationship between 24-hr time-use composition and cognition, with sociodemographic and health characteristics as additional predictors. Model estimates were used to estimate optimized cognition based on the interaction of 24-hr time-use composition and personal characteristics. Our 'ideal day' app delivers personalised 24-hr time-use recommendations tailored to individual characteristics. We demonstrate that personalisation of time-use interventions can be achieved in real time using open-source software.

Key words: time use, personalised medicine, digital tool, cognition

Introduction

Personalised (or 'precision') medicine approaches to healthcare move beyond the 'one size fits all' approach towards individualised prevention and treatment of illness [1]. Rather than using population averages to inform therapy, treatment and behaviour change, personalised approaches consider individual characteristics beyond age and sex, including genetic, environmental and lifestyle factors [1]. Whilst this approach is increasingly projected to be 'the future' of drug development (including applications in cancer treatment, pharmacogenomics and immunotherapy), lifestyle interventions which aim to optimise the balance of physical activity (PA), sleep and sedentary behaviours (SB) in the 24-hr day are seldom personalised to the individual. Instead, most approaches administer a universal "dose" (e.g., perform 20 minutes of walking, three times per week), or attempt to move all individuals closer to PA, sleep and/or SB guidelines which are also generalised.

An important but overlooked consideration is that the optimal 24-hr time-use composition (i.e., the optimal balance of PA, sleep and SB in the 24-hr day) for health outcomes may vary between individuals based on their current time use, health status, or sociodemographic "profile". That is, the unique combination of factors such as age, sex, mobility, health conditions, and socioeconomic status, as well as their current levels of PA, sleep and SB, may already have participants closer to, or further away from, their optimal day at the beginning of an intervention. Consequently, administering a universal intervention to a sample of individuals may not result in uniform intervention effects. Several key theories and methodologies have highlighted the potential value of personalising 24-hr time-use interventions for health. For example, the "Sweet-Spot" hypothesis postulated by Holtermann and colleagues [2] proposed that the optimal combination of PA, SB, and sleep for health likely differs between adults in physically active versus sedentary occupations. They argue that the generalised advice to "sit less and move more" may actually take adults who work in physically active occupations further away from their optimal 24-hr day, as their optimal day requires more time for recovery (SBs and sleep) than it does for those in sedentary occupations [2]. Similarly, the "Goldilocks Day" approach by Dumuid et al. [3] demonstrates that different health outcomes have different optimal days, thus determining someone's optimal day will require personalisation to their health priorities. For example, the optimal balance of PA, sleep, and SB looks different for cognitive health than it does for physical or mental health, meaning the optimal day is also dependent on how someone ranks these health domains (i.e., whether cognitive, physical or mental health are

of higher importance) [3,4]. Taken together, the Sweet-Spot and Goldilocks Day principles may also apply to the current health and sociodemographic profile of the individual.

Society today faces several pressing health challenges which may benefit from personalised prevention approaches, including dementia [5]. There are at least 14 established modifiable risk factors for dementia, many of which are potentially bi-directionally related PA, sleep and SB, such as obesity and depression. Additionally, physical inactivity is a risk factor for dementia [6]. It is likely that the optimal 24-hr time-use composition for minimising dementia risk for a 50-year-old male with high school-level education, hypertension, and a history of smoking, all of which have been identified as modifiable risk factors for dementia, looks different in comparison to another 50-year-old male with tertiary education, hypertension, and no smoking history. Despite the two individuals belonging to the same age group and both having a diagnosis of hypertension, the additional differences in modifiable dementia risk factors (education and smoking history) may change the relative impact that time-use behaviours have on dementia risk. That is, a higher amount of PA or different balance of time-use behaviours may be needed to offset the negative impacts of smoking and low education.

It is possible to compute the optimal 24-hr time-use composition for an outcome of interest (e.g., cognitive VS physical health) specifically for the average individual with given personal characteristics (e.g., age, sex) based on statistical models [7]. However, the challenge is how to effectively communicate behaviour change recommendations which are tailored to an individual participant in real time, such as in an intervention study. One solution may be *via* interactive interfaces which allow the user to set their own descriptors (e.g., age, sex, health status, current time use) and view the optimal day for their chosen health outcome. The Your Best Day interactive app developed by Dumuid and colleagues [4] achieves this: users select their sex, age, and current time use, and can then use interactive sliders to visualise the predicted effects of changing their time use on body fat percentage, psychosocial wellbeing, and academic performance in adolescents. In a dementia risk reduction context, digital tools are now widely viewed as acceptable and feasible approaches to facilitate behaviour change and enhance the delivery of preventative interventions. There are also an increasing number of digital tools available to compute dementia risk based on previous exposure to established risk factors [8]. However, to our knowledge, there are currently no interactive tools which generate a personalised and specific ‘prescription’ of physical activity, sleep and sedentary behaviour duration to improve health and reduce dementia risk.

Applying the principles of the Your Best Day app, the aim of the current study was to develop an interactive user interface to individualise 24-hr time-use recommendations for the *Small Steps* Study, a randomized controlled trial aiming to improve 24-hr time use for cognitive function (as a proxy for dementia risk) in community-dwelling older adults [9]. Using the UK Biobank [10] as our normative sample, we firstly aimed to identify the optimal 24-hr time-use composition for cognitive function outcomes across a range of sociodemographic and health profiles (i.e., across combinations of a range of modifiable and non-modifiable risk factors for dementia). Secondly, we developed a user interface (housed as an R Shiny app [11]) which allows users to input information about dementia risk factors (i.e., create their 'profile'), and view the optimal 24-hr day for cognitive function based on their profile.

Results

Participant demographics

A sample of 53,057 participants from the UK Biobank were included in this study (Table 1). Participants were 62.2±7.7 years of age, mostly female (56.7%), White (97.2%) and had predominantly college/university (46.6%) qualifications. The health profile of participants varied across modifiable dementia risk factors, with the most common risk factors including hearing difficulty (24.0%), history of hypertension (23.7%), regular alcohol consumption (23.4%), and history of depression (20.2%). On average, participants spent most of their 24-hr day in SB (9.6hrs, 40.0%) or sleep (9.0hrs, 37.5%), whereas active behaviours made up <25% of the day (LPA: 4.8hrs, 20.0%; MVPA: 0.5hrs, 2.1%). The number of participants per strata ranged from 2064 to 15303 (Supplementary Table 3).

Table 1. Descriptive characteristics of sample

Characteristic	**Level**	**Overall sample**
N		53,057
Age (years)		62.2 (7.7)
Sex (%)	Female	30,091 (56.7%)
	Male	22,966 (43.3%)
24-hr time-use composition	Sleep	542.7

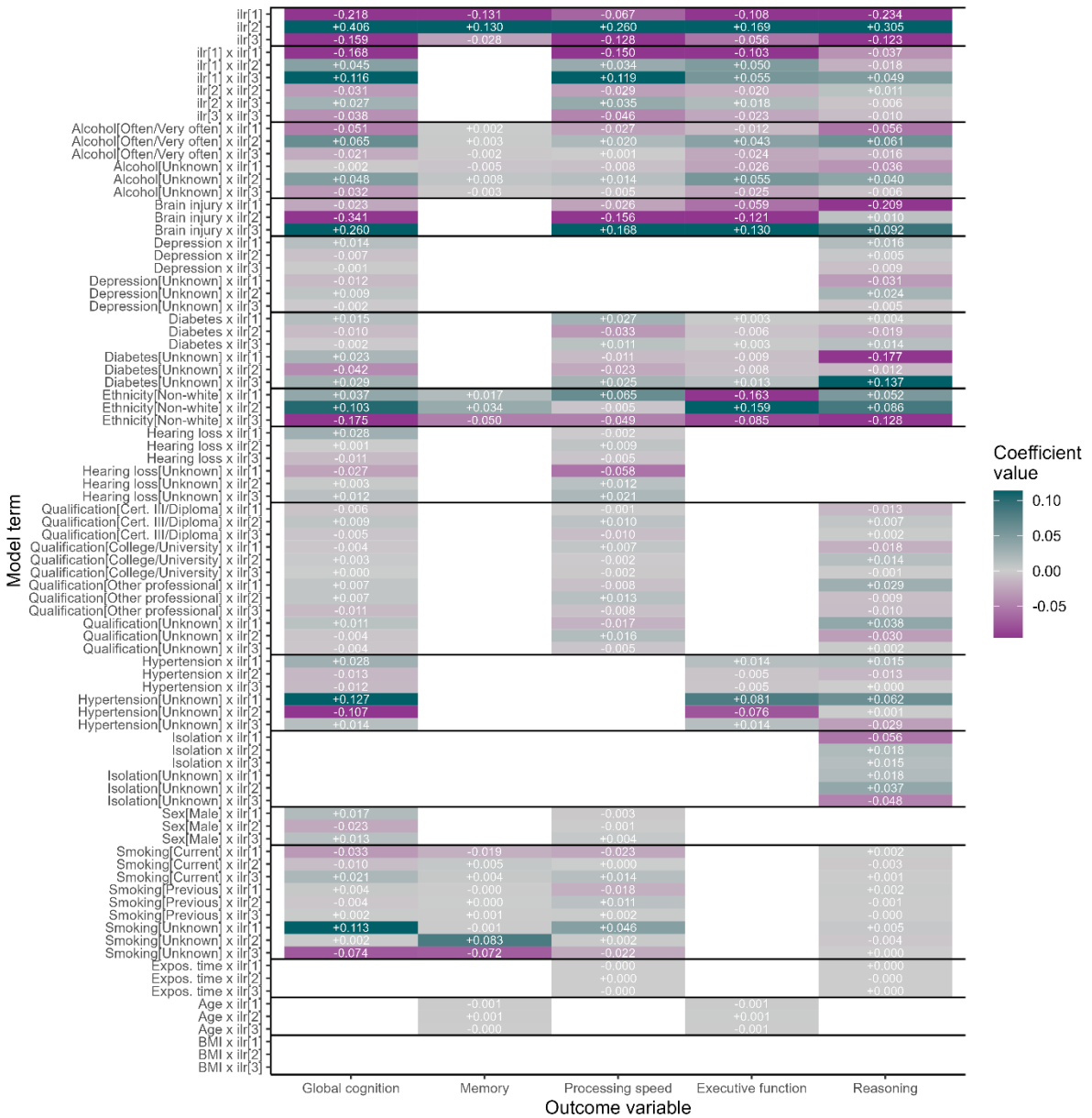
Characteristic	Level	Overall sample
	SB	576.9
	LPA	291.2
	MVPA	29.2
BMI		26.6 (4.5)
Highest qualification	High school	10,637 (20.0%)
	Certificate III or Diploma	5,805 (10.9%)
	College/University	24,742 (46.6%)
	Other professional qualification	8,092 (15.3%)
	Unknown	3,781 (7.1%)
Depression	Yes	10,734 (20.2%)
	No	9,141 (17.2%)
	Unknown	33,182 (62.5%)
Diabetes	Yes	1,665 (3.2%)
	No	51,295 (96.7%)
	Unknown	97 (0.2%)
Hearing difficulty	Yes	12,713 (24.0%)
	No	38,221 (72.0%)
	Unknown	2,123 (4.0%)
Hypertension	Yes	12,595 (23.7%)
	No	40,390 (76.1%)
	Unknown	72 (0.1%)
Social isolation	Yes	7,851 (14.8%)
	No	44,584 (84.5%)
	Unknown	622 (1.2%)
Smoking status	Current	3,447 (6.5%)

Characteristic	Level	Overall sample
	Previous	18,960 (35.7%)
	Never	30,532 (57.5%)
	Unknown	118 (0.2%)
Alcohol consumption (frequency)	Often/very often	12,415 (23.4%)
	Sometimes/never	26,641 (50.2%)
	Unknown	14,001 (26.4%)
History of traumatic brain injury		106 (0.2%)
Ethnicity	White	51,577 (97.2%)
	Non-white	1,480 (2.8%)
Days between accelerometry and cognitive testing		52.4 (232.2)

Model selection

Model coefficients for terms containing *ilrs* (i.e., main effects, higher order terms or interactions with time use) are displayed in Figure 1. Across all five cognitive outcomes, main effects were retained for *ilr*s, as well as interactions between *ilr*s and ethnicity, and *ilr*s and alcohol consumption. The remaining interaction terms containing *ilrs* were retained non-uniformly across cognitive outcomes. We note that predictor variables in group LASSO regression, and regularized regression more generally, are block standardised to zero vector mean and identity unit covariance, so when used to predict the (unit variance scaled) outcome, the predictors' strength of association with the outcome are directly comparable by magnitude of their associated coefficient. The complete model coefficient output (main effects, higher order terms and interaction terms for all variables) can be viewed in our GitHub repository (https://github.com/tystan/ukbb-cog-lasso).

Figure 1.



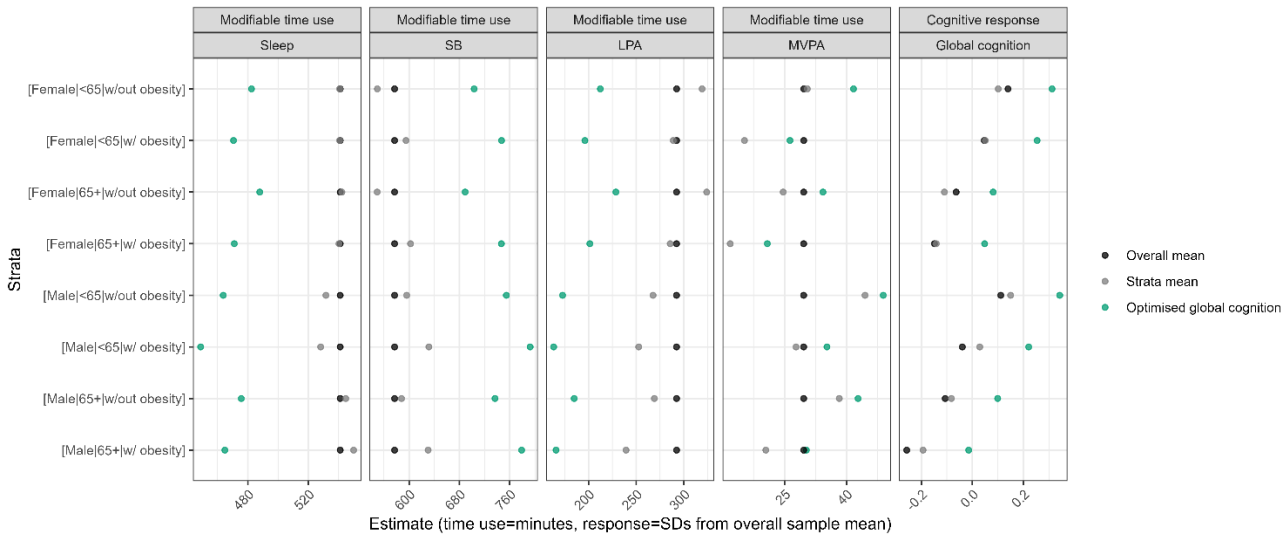
Optimal days for cognitive function

The optimal 24-hr days for cognitive function varied across strata and were further modified by health and sociodemographic characteristics. For ease of interpretation, we present findings on this variability by global cognition (i.e., general cognitive ability) first, followed by a comparison of optimal days across specific cognitive domains (memory, executive function, processing speed, reasoning) in a later section.

Figure 2 displays the estimated optimal 24-hr time-use composition for global cognition (across four compositional parts), and corresponding global cognition z-score across the eight age, sex, and BMI-defined strata. Across all groups, the optimal amount of SB and MVPA for global cognition was greater than the strata mean, whereas the optimal amount of sleep and LPA was lower than the strata mean. For example, the average (observed) time-use composition for females aged <65 years without obesity (top row of figure) was approximately 542 minutes of sleep (~9.0 hrs), 549 minutes of SB (~9.2 hrs), 318 minutes of LPA (~5.3 hrs), and 30 minutes of MVPA. Comparatively, the *optimal* day for global cognition within this stratum was 481.0 minutes of sleep (~8.0 hrs), 705.7 minutes of SB (~11.5 hrs), 213.9 minutes of LPA (~3.5 hrs), and 39.4 minutes of MVPA. Thus, to achieve an optimal 24-hr day for global cognition, on average, this stratum required approximately 60 minutes less sleep, 100 minutes less LPA, 150 minutes more SB, and 10 minutes more MVPA than the stratum's mean composition.

Across strata, the optimal amount of MVPA for global cognition varied the most by obesity status, whereby strata with obesity consistently required lower MVPA for their optimal day composition compared to those without obesity. Within the same age and sex classifications, differences in optimal MVPA by obesity status for global cognition ranged from ~12 minutes (females aged >65 years) to ~18 minutes (males aged >65 years). We note that the variability by obesity status is related to the constrained (feasible) time-use footprint containing lower MVPA in strata with VS without obesity – in other words, rather than individuals with obesity needing less MVPA to benefit cognition, their feasible limits of MVPA are lower due to the relationship between MVPA and BMI (see Supplementary Figure 8 for comparison of feasible limits of time-use behaviours across strata). Less consistent patterns were observed across age and sex classifications, and across other time-use behaviours.

Figure 2.



In addition to age, sex, and BMI, other health and sociodemographic factors altered the optimal day for global cognition to varying extents. Notably, presence/absence of TBI history had the strongest influence on optimal days, whereas additional health and sociodemographic factors (e.g., hypertension, smoking, alcohol consumption) had less impact on the optimal day within strata.

To demonstrate using a practical example, consider 'Person A' who has the following characteristics: female, aged <65 years, without obesity, college/university education, and no history of any health and sociodemographic factors (i.e., no hypertension, smoking, diabetes, depression, TBI, hearing loss, social isolation, or high alcohol consumption), with a current time-use composition of 7.8 hrs sleep, 13.0 hrs SB, 3.0 hrs LPA, and 0.2 hrs MVPA. To achieve their optimal day for global cognition, Person A would be recommended to increase their sleep (+0.2 hrs), LPA (+0.6 hrs), and MVPA (+0.5 hrs), and decrease their SB (-1.2 hrs). In comparison, Person B has the same baseline time use and belongs to the same stratum, but instead has high school education, history of hypertension, current smoking, diabetes, depressive symptoms, hearing loss, social isolation and frequent alcohol consumption. Despite a vastly different profile of health and sociodemographic characteristics, the recommended changes for Person B are very similar to Person A: increase their sleep (+0.3 hrs), LPA (+0.5 hrs), and MVPA (+0.5 hrs), and decrease their SB (-1.3 hrs). Notably, changing Person B's characteristics to also include a history of TBI dramatically changes the recommendations: increase LPA (+3.3 hrs) and MVPA (+0.2 hrs) and decrease sleep (-0.4 hrs) and SB (-3.1 hrs). It

is important to note that only 0.2% of the entire sample reported history of TBI (using the self-report variable), which may reduce confidence in these relationships.

The optimal day for cognitive function varied considerably across cognitive domains (Figure 3). For example, within one stratum (e.g., females, aged <65 years, without obesity) the optimal amount of each time-use behaviour for different cognitive domains varied as follows: optimal sleep varied from 467.0 minutes (7.8 hrs, memory) to 492.0 minutes (8.2 hrs, processing speed); optimal SB varied from 694.0 minutes (11.6 hrs, reasoning) to 705.7 minutes (11.8 hrs, global cognition); optimal LPA varied from 207.3 minutes (3.4 hrs, processing speed) to 228.0 minutes (3.8 hrs, memory); and optimal MVPA varied from 35.1 minutes (processing speed) to 52.5 minutes (reasoning).

Figure 3.

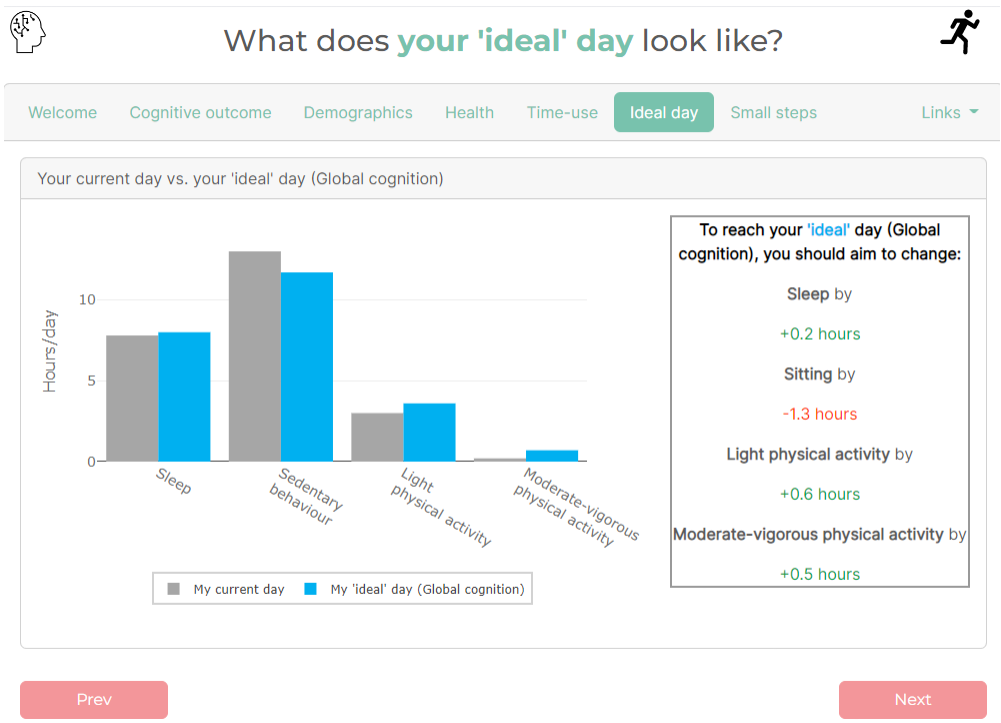
Interactive user interface for optimal day personalisation

The ‘ideal day’ interactive personalisation tool can be viewed at https://arena2024.shinyapps.io/ideal-day and the underlying code freely accessed on GitHub (https://github.com/tystan/ideal-day). We note that the use of ‘ideal’ rather than ‘optimal’ was chosen for the name of the *Small Steps* study app, in response to preferences indicated during the co-design process[12]. For consistency, we will continue to refer to this app as the ‘optimal day’ tool herein. The tool is divided stepwise into six main tabs. First, participants can select the cognitive outcome they are interested in predicting for (global cognition, memory, processing speed, executive function, or reasoning). In the ‘Demographics’ tab, the user is asked to input their current age (years), current weight (kg) and height (cm) using free-text boxes, as well as their sex and highest qualification from pre-defined options. The ‘Health’ tab then asks the user a series of multiple-choice questions (with mostly ‘yes’, ‘no’, or ‘unknown’ response options)

about modifiable dementia risk factors including history of hypertension, type 2 diabetes, depression, social isolation, hearing loss, TBI, alcohol consumption and tobacco smoking. Finally, users are required to enter their current time use ('Time-use' tab) using free text boxes, entering the number of hours per day they spend in sleep, sitting, light physical activity, and moderate-vigorous physical activity. Using these inputs, the tool then displays the user's current day (i.e., current time-use composition) next to their 'optimal day' in the 'Ideal day' tab.

In the example displayed in Figure 4, the user is interested in determining the optimal day for their global cognition. Their current time use is 7.8 hrs sleep, 13.0 hrs sedentary behaviour, 3.0 hrs LPA and 0.2 hrs MVPA per day, and based on the optimisation analysis, to achieve their personalised 'optimal day' the user is advised to increase time in sleep, LPA and MVPA, and decrease time in sitting. As the Small Steps intervention aims to help participants make small, beneficial changes in behaviour which suit their preferences, needs and constraints, the final component of the Shiny app (the 'Small Steps' tab) dynamically reports on the whether the relative direction from current time-use to the selected change in time-use (e.g., increasing 10 min of MVPA –and decreasing sleep by 10 min of sleep) is aligned with the theoretical direction of current time-use to the optimal time-use. This feedback was operationalised using a traffic light system, where green lights indicated the proposed time-use change is moving towards the optimal day, and red lights indicated moving away from the optimal day. The methods underpinning this feature are beyond the scope of the current paper, and will be described elsewhere.

Figure 4.



Discussion

This study described the development of a novel interactive user interface which could be used to generate personalised behaviour change recommendations for individuals in real time. In our proof-of-concept example, we showed that the optimal balance of sleep, SB and PA in the 24-hr day for cognitive outcomes (i.e., the 'optimal day') differed depending on the health and sociodemographic profile (i.e., modifiable dementia risk factor profile) of participants in a sub-sample from the UK Biobank. We found that 24-hr time-use composition was associated with all five cognitive outcomes (global cognition, memory, processing speed, executive function and reasoning), and that the optimal day for cognitive function varied across strata, and across cognitive domains. For example, to achieve 'optimal' global cognition, the recommended change in time use from observed to optimal days varied widely across age, sex, and BMI-defined strata (using the 'average case' participant): recommended change in MVPA ranged from +3 minutes to +10 minutes; recommended change in LPA ranged from -66 minutes to -105 minutes; recommended change in SB ranged from +96 minutes to +207 minutes; and recommended change in sleep ranged from -60 minutes to -94 minutes. The predicted difference in global cognition z-score between observed and optimal days across all strata was on average +0.2 SDs, whilst for other cognitive domains, the average predicted difference

between observed and optimal days ranged from +0.05 to +0.2 SDs. Finally, within each of the stratum, the relationship between 24-hr time-use composition and cognitive performance was further altered by other health and sociodemographic characteristics, such that the optimal day (target durations of daily activities) generated by our interactive app varied depending on user inputs. These potentially substantial differences in optimal day predictions demonstrate the importance of personalising 24-hr time-use interventions for health outcomes (e.g., cognitive health in older adults).

Our study builds on the formative work of recent studies that have published “ideal”, “optimal”, or “Goldilocks” days for a single health outcome, or population [3,7,13]. We extend this work in five important ways, made possible by the large underpinning dataset. First, we developed a sophisticated data-driven model selection procedure using group LASSO regression that considered all main effect candidate predictors, interactions and second-order polynomial terms. This allowed us to consider more complicated multiplicative relationships between time use, health and sociodemographic characteristics (e.g., modifiable dementia risk factors) without model overfitting. The group LASSO method overcomes the violation of the assumption of invariance under the choice of *ilr* transformation, which would occur if a single log-ratio is retained while others are discarded in standard LASSO regression [14]. Second, to address the same issue of invariance under alternate log-ratio transformations, we implemented a multivariate scaling method for the log-ratios. Third, we stratified our analyses by key characteristics (age, sex, and BMI) which showed strong interactions with the time-use log-ratios, ensuring differences in associations between these strata would be reflected in our final optimal day predictions. Fourth, to ensure our models best represented the empirical relationships present in the data, we tested for all pairwise interactions between included predictors, and for non-linear relationships. Fifth, we present a new method (“constrained ellipsoid fencing”) to improve how the empirical time-use footprint is selected for prediction of optimal days. To restrict the sample of possible ‘optimal days’ to a more feasible range, previous methods applied univariate constraints (e.g., restricting at the 3rd standard deviation) to each time-use behaviour separately [3] . However, this approach is incongruent with the compositional approach, and results in extrapolations into unsampled territory where there are few or no empirical data points. Constrained ellipsoid fencing presents a more suitable approach to restrict the 24-hr time-use footprint which is multivariate in nature (rather than applying a univariate approach). Taken together, we present a novel time-use optimisation pipeline which can be replicated for alternative outcomes, populations and predictor variables using our published code (available on GitHub).

We contribute new findings to a growing literature regarding the associations between 24-hr time-use composition and cognitive function in late adulthood. We found that 24-hr time-use composition was associated with cognitive function in older adults, which is congruent with some previous compositional studies [15-17], but not all [18-21]. Patterns across the predicted optimal days in our study suggest that, compared to the "average" individual in each of the 8 age/sex/BMI strata, better cognition was associated with more time in MVPA and SB, and less time in LPA and sleep (relative to the mean time-use composition of the strata).

Our findings for MVPA and LPA are consistent with many previous non-compositional and compositional studies [22-24], which report cognitive benefits of higher intensity PA, and negative albeit largely inconclusive association between LPA and cognition. We provide evidence that light intensities of PA may not be sufficient to provide cognitive benefits, as these take time from more beneficial activities such as MVPA. Our analyses show that SB also has beneficial associations, up to an optimal duration, after which benefits appear to wane. Thus, when aiming to optimise cognition, MVPA and SB may compete for time-shares within the 24-hr time window. Our findings for SB contribute to a mixed literature, whereby some studies have reported beneficial associations between SB and cognition [16], whilst others have found negative (or no) associations [25,26]. It is increasingly recognised that the type and context of SBs may alter their association with cognitive outcomes [25,27]. For example, our recent work among older adults demonstrated that cognitively engaging SBs (e.g., reading, computer use) are beneficially associated, whereas cognitively passive SBs (e.g., TV watching) are detrimentally associated with cognition [16]. As our SB variable was derived from accelerometry in the current study, we were unable to differentiate between cognitively engaging and passive sedentary time. Notably, the mean SB time in our UK Biobank sample was considerably lower (~9.6hrs/day) than other samples exploring similar relationships in older adults (e.g., 11hrs [19] to 12hrs [15]). It is likely that this contributed to the finding that optimal days required an increase in SB across all strata. Finally, for all strata, we found that optimal sleep duration was lower than the mean sleep duration. The extant literature suggests there is an inverted U-shaped relationship between sleep and cognition, whereby long or short sleep duration (e.g., <6 or >9 hrs) is associated with reduced cognitive performance [28-30]. In the current sample, mean sleep duration ranged between 8.8 and 9.2 hrs across strata, which is close to the upper bound of the range of sleep durations associated with better cognition in aforementioned studies. However, it is important to note that the Biobank sleep measure did not account for nighttime awakenings, or time awake in bed. Thus, longer sleep durations may reflect poorer sleep efficiency, where relatively longer durations of the "sleep" variable are spent lying awake in bed rather than asleep. Moreover, the

derived time-use behaviours may have subsequently overestimated time in sleep and underestimated time in SB (which ranged between 9.2 and 10.5 hrs/day in this sample).

Our findings provide evidence that different population sub-groups require different balances of sleep, SB, LPA and MVPA in the 24-hr day for cognition, and unique combinations of sociodemographic and health characteristics may further adjust the 'optimal day' for cognition. This supports the Sweet Spot Hypothesis, and suggests that 'one-size-fits-all' approaches to time-use recommendations may not confer equitable benefits across a sample of participants. In our study, the patterns of associations were relatively consistent between the strata (i.e., for all strata, the optimal days had more MVPA and SB, and less LPA and sleep than the strata average). The differences between strata were in the recommended durations of the behaviours, which was directly linked to the bounds of the time-use footprint considered "feasible" for each of the strata. For example, the maximum duration of MVPA considered feasible for females aged >65 years with obesity was 110 minutes (minimum = 5 minutes), compared to almost double (205 minutes; minimum = 10 minutes) among males aged <65 years without obesity. Constraining the time-use footprint to a feasible range is crucial to producing behaviour change recommendations that are meaningful and achievable for the target population.

Our study describes new methods for computing personalised 24-hr time-use recommendations via an interactive interface. Time-use recommendations have, over the last two decades, moved from a focus on individual behaviours (PA, SB, sleep) towards recommendations encompassing the whole 24-hr day (e.g., Canadian 24-Hour Movement Guidelines for Adults [31]). However, even the most recent guidelines are merely composites of separate sets of recommendations for each of the movement behaviours. Furthermore, the guidelines apply to all people within the designated age bands, agnostic to other personal characteristics and current behaviours. Understanding the optimal balance and/or trade-offs across the 24-h day needed to maintain health has been the focus of an increasing number of studies in the past decade [32]. The app presented here goes beyond the one-size-fits-all approach to optimising the balance of PA, sleep and SB in a true 24-hr day, and may be an important next step towards personalised approaches to chronic disease prevention.

With relevance to the cognitive aging and dementia prevention field, interventions (including multi-domain trials) which have incorporated a component of PA have yielded mixed findings [33]. It is possible that these mixed findings may be, at least in part, due to the lack of consideration of trade-offs being made with other components of the day (sleep and SB), or the lack of

personalisation based on previous exposures to other modifiable risk factors for dementia. Above all, calculating and then communicating optimal days which are personalised to the individual's sociodemographic and health characteristics is complex. Our app presents a potential solution by providing an accessible interface, co-designed with older adults and health professionals, to generate and translate 24-hr activity interventions that are tailored to the individual. However, we emphasise that the current iteration of the app is a proof-of-concept and requires further development and testing in community and clinical settings before wider implementation or public deployment.

This study has a number of strengths. We used robust model selection procedures to avoid over-fitting models, and achieve a balance between complexity and understanding. This study included a large population-based sample, and 24-hr activity and sleep data were collected using device-based methods (accelerometry) which may be less susceptible to recall bias or inaccuracy in older populations. We explored several cognitive outcomes, which strengthens evidence of domain-specific associations between 24-hr time-use composition and cognitive function in older adult populations. Finally, the user interface of the app was co-designed with community-dwelling older adults and health professionals for whom the app was initially intended [12]. As a result, the user interface is accessible and easy to interpret, avoiding complex language. There are limitations which must also be acknowledged. Cross-sectional data were used to estimate relationships between 24-hr time-use composition and cognitive outcomes. Extending the methods presented here by using longitudinal data would also allow researchers to explicitly consider the effect of within-person changes in time use in addition to the between-person differences that the current recommendations are based on. Moreover, due to the cross-sectional nature of these data, we cannot rule out the potential for reverse causation, whereby cognition influences time use. Causal evidence is needed to guide such lifestyle prescription tools, which due to the model-agnostic pipeline utilised in this study, can be implemented in future iterations. Twenty-four-hour time-use data were measured using wrist-worn accelerometers which are not considered the gold standard for measuring postural changes (i.e., differentiating between sitting and sleeping). It is possible that some SBs (e.g., time awake in bed) were classified as sleep, resulting in the over-estimation of time in sleep. This potential discrepancy may have contributed to the findings that 1) participants engaged in a lower-than-expected amount of SB per day (9hrs) compared to other cohorts of similar age, and 2) more time in SB was associated with better cognitive function. It is also acknowledged that the measurement properties (e.g., accuracy or validity) of instruments used to measure lifestyle factors considered in predictive modelling (e.g., smoking history, alcohol consumption) can

influence optimal day recommendations, so beyond this proof-of-concept example, future iterations must carefully consider the tools used to measure such predictors. Additional factors known to relate to time use and/or cognitive performance, including diet, social engagement, and genetics were not included in our models. Extending these analyses to understand the synergistic effects of time use (including elements of time use beyond duration, such as context) and diet for cognitive performance is an area of opportunity for future work. Moreover, accounting for genetic risk factors for dementia (as well as health and sociodemographic characteristics) may enhance the precision and potency of personalised time-use prescriptions for brain health. Finally, the UK Biobank sample used in this study are relatively homogenous in their characteristics and don't reflect the most at-risk groups for cognitive decline and dementia (particularly Alzheimer's disease). Consequently, the influence of health and sociodemographic characteristics on the 'optimal day' for cognitive performance may have been underestimated in the current sample due to limited variance in these predictors (e.g., years of education/highest qualification). This approach to personalising 24-hr time-use interventions should be explored in datasets whereby the population are more representative of at-risk populations (e.g., those from low-to-middle income countries, with greater ethnic diversity) [6,34].

This first-of-its-kind, proof-of-concept study provides important foundations for future time-use personalisation research and intervention studies to build upon. We anticipate several key future directions for this work. First, as this analysis pipeline is able to be replicated for alternative study types (e.g., time-to-event analyses), future studies should explore the utility of time-use personalisation for clinical outcomes, such as onset of Alzheimer's disease or other chronic diseases. Second, with relevance to the association between time-use composition and cognitive performance, these relationships should be explored longitudinally and account for additional factors which may have confounding effects, such as diet, social engagement, or genetics (e.g., carriage of dementia risk genes such as apolipoprotein E ε4). Third, future versions of this time-use optimisation pipeline should incorporate measures of prediction uncertainty (i.e., to indicate confidence in 'ideal day' recommendations). Fourth, the pipeline can be extended to create personalised 'optimal days' for multiple response variables concurrently (i.e., the Goldilocks method [3]). Fifth, future studies should consider the context in which activity occurs (e.g., cognitively active vs. cognitively passive SB; MVPA occurring in work vs leisure) to further personalise optimal days for health.

In the long term, we envision that such a tool could be implemented in health practice, whereby clinicians could work with patients to iteratively update their risk factor profile in order to update

their ‘optimal day’ goals over time, and as their health status changes (e.g., BMI, presence/absence of chronic conditions). Application of this tool in clinical settings would require further development through co-design with clinicians and other relevant end-users, and extension to clinically relevant outcomes (e.g., Alzheimer’s disease onset, or cardiovascular disease). Future versions of this tool may be strengthened through integration of artificial intelligence-driven adaptive feedback or multimodal data integration (e.g., continuous monitoring of 24-hour time use through connected wearables, rather than ‘current day’ inputs based on a single 7-day average). Based on the ‘average’ participant in this sample, we found that the predicted benefit to global cognition (z-score) when moving from observed to optimal days was +0.2 SD. If this approach were used in populations with greater opportunities for improvement in their time-use patterns (e.g., less active populations) or with poorer cognition (i.e., with lower observed cognitive test scores), the predicted differences between observed and optimal days, and therefore opportunities for cognitive gain, may be even greater.

Methods

Study design and participants

Data used in this cross-sectional study were from the UK Biobank (application no. 62254), a large prospective cohort study of ~500,000 participants aged >40 years at time of recruitment in 2010 [10]. The sample for this study were limited to UK Biobank participants who met the following criteria: accelerometry data were marked as ‘valid’; accelerometry data did not have a data problem indicator; at least four of five cognitive tests included in this study were completed; a diagnosis of dementia, organic amnesic syndrome, delirium, systemic atrophy affecting the central nervous system, extrapyramidal or movement disorder, other degenerative disease of the central nervous system, demyelinating disease of the central nervous system or blindness was not recorded prior to either completing the cognitive tests or wearing the accelerometer; and no indication that participant was unable to walk. A complete list of inclusion and exclusion criteria are displayed in Supplementary Table 1.

Study measures

A range of sociodemographic and health variables which have been identified as modifiable dementia risk factors as per the 2020 Lancet commission report [34] were extracted from the assessment centre data (initial visit) for consideration in our model selection procedures. A

detailed list of included variables, their UK Biobank field codes and data re-classification protocols (where applicable) is available in Supplementary Table 2. As the final behaviour change tool (detailed below) was initially intended for use in an Australian context, where necessary some variables (e.g., education/highest qualification) were re-levelled to align with Australian classifications. Final variables included age, sex, ethnicity (levels = “White”, ”non-White”), highest qualification (levels= “high school”, “Certificate III/Diploma”, “College/University”, “Other professional qualification”), alcohol consumption (levels= “sometimes/never”, “often/very often”), smoking status (levels=“never”, “previous”, “current”), history of depression (levels=“yes”, “no”), hearing difficulty (levels=“yes”, “no”), history of hypertension (levels=“yes”, “no”), history of traumatic brain injury (levels=”yes”, “no”), type 2 diabetes status (levels=“yes”, “no”), body mass index (BMI; levels=”overweight”, “not overweight”), and social isolation (“yes”, “no”). For all variables, missing data were recoded as ‘unknown’ (i.e., some dichotomous variables had three levels: yes, no, unknown).

Average daily times spent in sleep, SB, light intensity PA (LPA) and moderate-vigorous intensity PA (MVPA) were obtained from the derived accelerometry data [35] within the UK Biobank (field codes are presented in Supplementary Table 2). These four variables were conceptualised as a daily time-use composition, summing to 1,440 minutes. The time-use variables are perfectly multi-collinear – because together they always sum to 1,440 minutes, increases in one variable must be accompanied by compensatory decreases in the other variable(s). Consequently, the time-use variables are co-dependent, meaning it is not appropriate to include them as independent predictors in a multiple regression model. Compositional data analysis (CoDA) overcomes this issue by applying a log ratio transformation to the raw compositional variables [36]. The log ratio transformation expresses the compositional data as a set of isometric log ratio coordinates (*ilrs*). The *ilrs* capture all the relative information about the compositional parts, but unlike the raw compositional parts, they are not constrained to sum to a total, nor are they perfectly multi-collinear. The *ilrs* can be used to represent the 24-hr time-use composition in traditional statistical models.

Briefly, to create *ilrs*, time spent in all time-use behaviours must be greater than zero minutes. Thus, zero values in any compositional parts (sleep, SB, LPA, MVPA) were imputed assuming censored data (values below the threshold of detection) using a linear model-based imputation of log ratios of the components, iteratively improved via the Expectation-Maximisation algorithm (*lrEM* function in the zCompositions R package [37,38]), with the remaining behaviours reduced by the small, imputed value proportionally. The raw values were truncated at ±0.5% of their

empirical distributions to mitigate the undue influence of extreme values. The four *compositional parts* (sleep, SB, LPA, MVPA) were then expressed as a set of three *ilr* coordinates using a sequential binary partition *ilr* basis representing the following quantities (ignoring normalizing constants): the first *ilr* represented the log-ratio of sleep to the geometric mean of the remaining three behaviours (SB, LPA, MVPA); the second *ilr* excluded sleep, and represented the log-ratio of the next behaviour in the set (SB) to the geometric mean of the remaining two behaviours (LPA and MVPA); and the final (third) *ilr* represented the log-ratio of LPA to MVPA. Together, the three *ilr* coordinates represent 24-hr time-use composition as a set of linearly independent predictors in regression models.

Based on previous evidence that both 24-hr activity and sleep patterns and ageing relate to cognitive function in a domain-specific way [22,39], we tested associations across four cognitive domains including memory, reasoning, executive function, and processing speed, and computed a global cognition variable to represent overall cognitive ability. Broadly, for the purpose of this study (according to the tests used to create composites): *memory* is defined as the ability to encode, store, and retrieve or recall information accurately (e.g., words that were read aloud) following a time delay; *reasoning* is the capacity to problem solve using logic and reasoning ability, independent of one's prior knowledge (also referred to as fluid intelligence); *executive function* is the ability to effectively utilize or manage multiple cognitive resources efficiently to solve problems in real time, and/or plan for the future; and *processing speed* is the ability to perform tasks (ranging from simple to complex) accurately and quickly (i.e., under time pressure) [40].

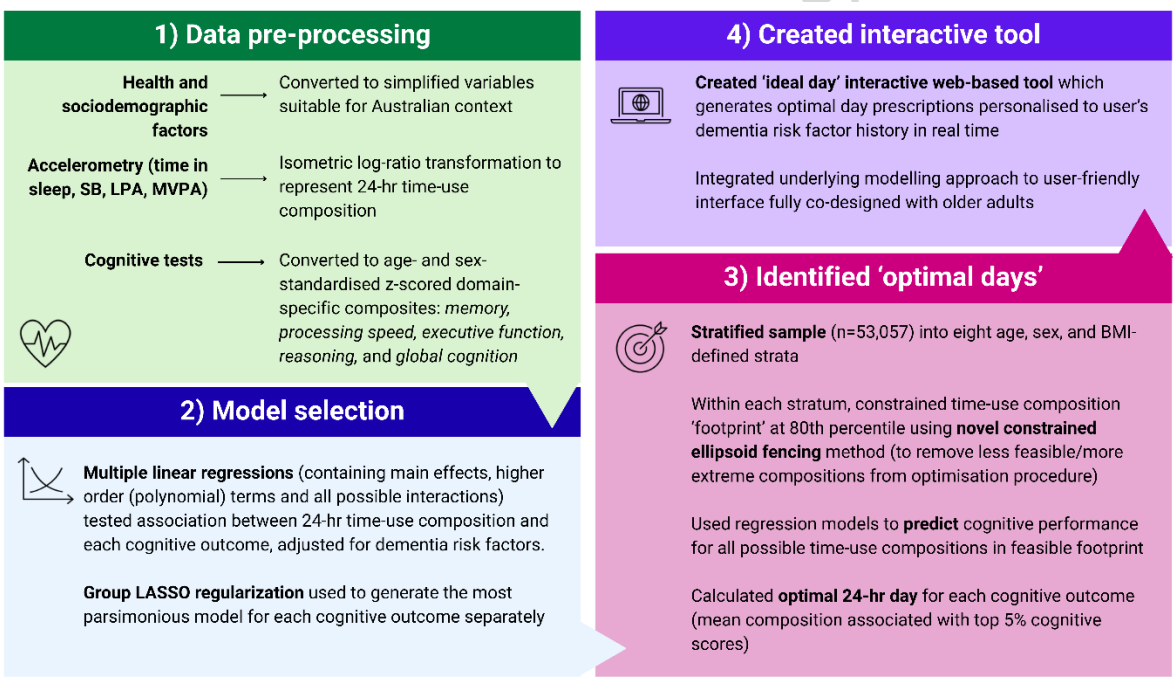
To create composite scores which reflect performance in these domains, several web-based cognitive tests collected during the UK Biobank online follow-up were included, including Numeric Memory, Pairs Matching, Fluid Intelligence, Trail Making (A and B), and Symbol Digit Substitution. Supplementary Table 2 presents the individual outcome measures extracted from these tests and how they were combined into composite scores to represent the four domains using groupings based on a previous UK Biobank study [41]. To create the composites, we first reverse-scored Trail Making A, Trail Making B and Pairs Matching outcomes so that for all included measures, higher scores represented better performance. We then undertook the following steps to normalise the distributions of the measures: Trail Making A and B scores were truncated at 300 seconds and log-transformed; Pairs Matching scores were truncated at -7 seconds; and Symbol Digit Substitution scores were truncated at 31. Individual measures were z-scored using age and sex standardisation (age= <65 years, >65 years; sex= male, female).

Finally, composite scores were created by averaging z-scores (where applicable), and an overall composite score (global cognition) was created by averaging the four z-scores. Supplementary Table 2 outlines test outcomes and their corresponding cognitive domains.

Data analysis

All analyses were conducted in R Statistical Software (version 4.3.1 [42]). Full R codes are published on GitHub (https://github.com/tystan/ukbb-cog-lasso). Figure 5 provides a simplified schematic overview of the analytic workflow, detailed in the following sections.

Figure 5.



Model selection by regularization

To model the associations between 24-hr time-use composition and cognitive outcomes, regularized linear regression models were fit with each of the five cognitive function measures as the outcome variable and the following candidate predictors (prior to shrinkage): continuous and discrete main effect predictors (time-use log-ratios (ilrs) and all sociodemographic and health factors); all pairwise main effect interactions; and additional squared continuous main

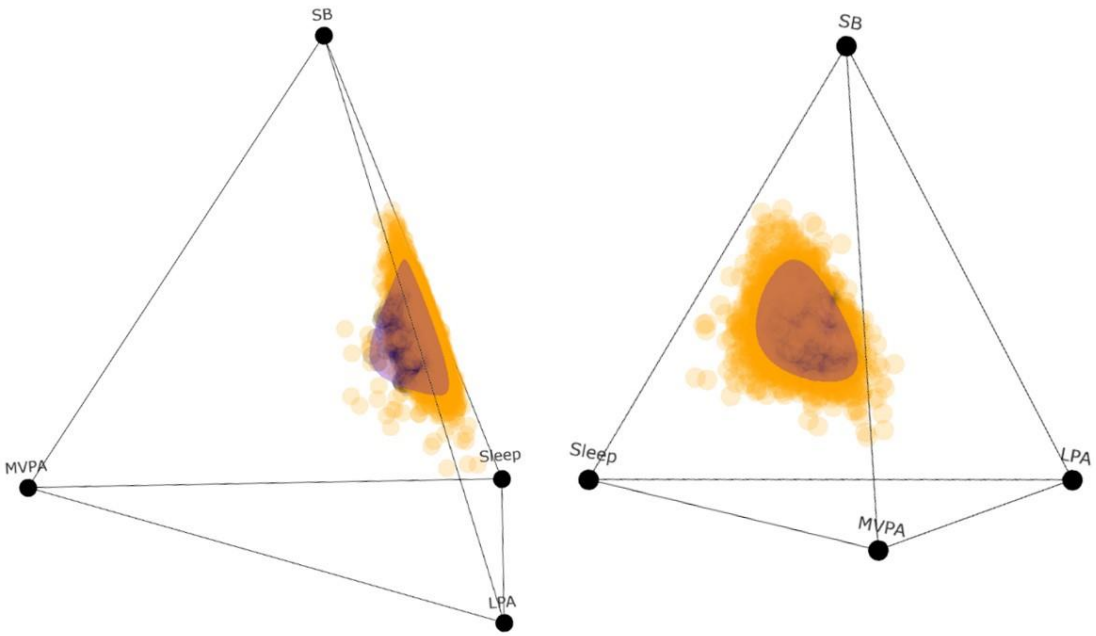
effects (i.e., polynomial terms degree 2). To reduce non-informative candidate predictors and avoid overfitting (model selection), Least Absolute Shrinkage and Selection Operator (LASSO) regularization was used. LASSO regression is a coefficient shrinkage method which aims to produce a parsimonious model based on a subset of the potential predictors that are interpretable and related to the outcome, by penalising the sum of the absolute values of a model's variable coefficients, forcing some coefficients to exactly zero and therefore to become omitted from the model [43]. However, because the *ilr* variables were required to be treated as analytically inseparable variables (in order to represent the 24-hr time-use composition), in addition to having many categorical variables with more than two levels, we specifically implemented group LASSO models [44] using the grpreg R package [45]. The group (or "block") extension of LASSO regression allows multiple predictor variables to be treated as an inseparable group – the shrinkage is applied block-wise, instead of individually, on the prespecified groupings of variables. Such an approach is required to ensure the invariance of the specific *ilr* basis chosen, but can also be useful to regularize categorical variables with three or more levels (resulting in two or more contrast dummy coded variables) as an inseparable group that the model would otherwise not know are intrinsically related. By applying a group-specific penalty, the coefficients in the group are both shrunk at a group level (e.g., the group of categorical level contrasts) as well as individually [46]. To this end, the *ilrs* were also treated as a group after centring and an angle preserving rotation was applied (to mitigate the issue of computing different shrinkage results dependent on the *ilr* basis chosen [47]). Similarly, the higher order terms were specified as groups, incorporating each crossed (or squared) sub-term in the case at least one categorical variable or *ilr* in the interaction (or squared) term was retained after shrinkage.

Despite group-specific penalties being sought, the model formulation can be equivalently re-expressed with a single penalisation parameter, λ, with the associated sum of the product of the square root of the group size and the Euclidean norm of the group variable's coefficients [44]. To determine an empirically derived optimal penalty value, λ*, of the shrinkage procedure, we performed a ten-fold cross-validation over a grid of potential λ values seeking the one that minimises the model's predictive mean squared error (MSE) of the model predicted values compared to observed values. Supplementary Figure 1 displays the derived λ* and corresponding MSE for each of the cognitive variables.

Identifying 'optimal' days for cognition

Due to the known mediating effects between *ilrs* (time use) and age, sex and BMI, the data were stratified into 8 mutually exclusive groups based on the following categories: age (<65 years, ≥65 years), sex (male, female), and BMI (with obesity= ≥30, without obesity= <30). Extending the methods outlined in Dumuid et al [3], the models described in the previous section were used to predict cognition for a "time-use footprint" that was considered feasible and realistic for each of the 8 population strata. To restrict the time-use footprint to realistic values, and to avoid extrapolating from the highest density of sampled time-use data, we used a grid of all possible time-use compositions with 5-minutes spacings constrained within the empirical distributional (multivariate Gaussian) quantiles of the strata-specific sampled data in the *ilr*-space. This was achieved using "constrained ellipsoid fencing", a novel method for which codes and an accompanying written tutorial are available at https://github.com/tystan/ukbb-cog-lasso. In brief, constraining a multivariate (compositional) search space to more feasible limits has previously been achieved by truncating the distribution of each individual time-use behaviour at ± 3 standard deviations from the mean. However, this often results in a mismatch between the search space and the actual distribution of data points, as the approach applies a univariate method to multivariate data (i.e., time-use composition). *Constrained ellipsoid fencing* restricts the search space to the empirically estimated multivariate normal contour limits at a specified percentile (depending on the distribution of the underlying data). In the current study we restricted the search space at the 80th percentile after assessment of marginal (univariate), pairwise, and multivariate normality by way of visual checks (where possible in lower dimensions), and cumulative quantile plots. Compared to other alternatives (e.g., restricting at the 90th percentile), restricting at the 80th percentile achieved better coverage of empirical data and avoided being overly restrictive (e.g., removing possible 'optimal days' that may be aspirational but still possible for some). Figure 6 demonstrates, for one of the stratum, the relationships between the sampled time-use compositions, where points are either classified as within or outside the *ilr*-derived constrained ellipsoid fencing when transformed back to the compositional scale and presented in the 4-simplex tetrahedron (constrained, constant sum space) in which they reside. Approximately 80% of the points are within the ellipsoid fencing as is expected if the (*ilr*) data are from an approximately multivariate Gaussian distribution.

Figure 6.



Optimal cognitive function was operationalized as the top 5% of the cognitive scores predicted by the models over the given constrained grid and specific person inputs [7]. The optimal 24-hr time-use composition for cognitive function was conceptualised as the compositional mean (geometric mean, adjusted to sum to 1,440 minutes) of the time-use compositions (sleep, sedentary time, light physical activity, MVPA) associated with the top 5% of predictions [7]. As models for the relationship between time-use composition and cognitive function also included interactions between various sociodemographic and health factors, the estimated optimal day varied depending on the values on these covariates. The optimal day for global cognition for the "mean" or "average" person in each of the strata is presented in the main manuscript, but for further personalisation of the optimal day estimate according to the value of the covariates, real-time estimation applying the specified covariate values to the model coefficients is made possible via our Shiny app interface (detailed below).

Developing the interactive user interface

The R "Shiny" package [11] was used to program an interactive interface (app) that can be freely accessed in a web browser via a URL, without the need to install R or any other additional software. Our Shiny app has three components (i.e. R scripts) that communicate with each other: (1) the user interface (ui.R), which determines the appearance of the app and how the

user enters information; (2) the server (server.R), which takes input provided by the user interface, sends it for computation, and then returns results back to the user interface; and (3) the global script (global.R), which defines the variables and functions accessible for both the user interface and server. The R scripts used for our Shiny app can be found in a separate GitHub repository (https://github.com/tystan/ideal-day). The LASSO regression coefficients from the compositional models were extracted for the app's global script. To determine the optimal day for user-specified covariates (i.e., their 'profile'), the app's user interface requests the user's sociodemographic and health details. From this, the app matches the user to one of the eight (age, sex, and BMI) defined strata. It then uses the user's remaining inputted sociodemographic and health variables, and every possible time-use composition within the feasible range for the user's stratum, to predict cognition. The app then extracts the top 5% of predictions and calculates the mean time-use composition associated with these top 5% of predictions, i.e., the optimal day. The workflow underpinning our Shiny app is displayed in Supplementary Figure 2.

The user is required to enter their current 24-hr time-use composition. In the case of the *Small Steps* study [9] for which this app was created, these values are derived from wrist-worn accelerometers worn by the participant prior to their initial visit (i.e., 7-day average of time spent in sleep, SB, LPA and MVPA from Fitbit watch). Following the user input of their current day, a bar plot is generated which displays the user's current 24-hr day (mins/day of sleep, SB, LPA and MVPA) compared to their 'optimal' 24-hr day. Feedback is provided about the changes required to reach that day from their current day (e.g., -10 minutes sleep, -20 minutes sedentary behaviour, 0 minutes light physical activity (i.e., no change), +30 minutes MVPA).

The appearance and functionality (e.g., colours, font sizing, wording) of the Shiny app was informed by older adults from the general population (n=8) and allied health professionals (n=4) through a series of co-design workshops conducted as part of the *Small Steps* study (Ethics ID 205377). During two of the six workshops, co-designers were shown prototypes of the Shiny app and provided feedback on visual elements and interpretability of the data and figures presented. Supplementary Figures 3-7 show de-identified examples of feedback obtained and iterations made across several versions. A full description of the co-design process can be viewed elsewhere [12]. Formal usability testing of the app is underway, and will be presented in a future manuscript.

Data availability

The data that support the findings of this study are available from the UK Biobank but restrictions apply to the availability of these data, which were used under licence for the current study, and so are not publicly available.

Code availability

The underlying code for the data preparation, cleaning, analysis and diagnostics for this study is freely accessible on GitHub and can be accessed via this link (https://github.com/tystan/ukbb-cog-lasso) in addition to the 'ideal day' interactive personalisation tool hosted at https://arena2024.shinyapps.io/ideal-day/with the associated underlying code also freely accessed on GitHub too (https://github.com/tystan/ideal-day).

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Author contributions

MM conceptualized the study, supported data analysis, and prepared the manuscript. TS conceptualized the study, conducted data analysis and contributed to manuscript development. TO and AM contributed to manuscript development. AS led the co-design of the app interface, conceptualized the study, and contributed to manuscript development. DD conceptualized the study, supported data analysis, and prepared the manuscript. All authors read and approved the final manuscript.

Competing interests

All authors declare no financial or non-financial competing interests.

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TABLE 1 LEGEND: Mean and standard deviation (SD) are presented for continuous variables, and count and proportion (n(%)) are presented for categorical variables for the overall sample. BMI=body mass index; SB=sedentary behaviour; LPA=light intensity physical activity; MVPA=moderate-to-vigorous intensity physical activity. A positive value for days between accelerometry and cognitive testing indicates that accelerometry measures occurred later than cognitive testing.

FIGURE 1 LEGEND: Isometric log-ratio (*ilr*) main, squared, and interaction (between health/sociodemographic characteristics and ilrs) coefficients (y-axis) in the group LASSO model fits for each outcome (x-axis) are presented by text and coloured cells. Blank cells (white spaces) indicate model terms that were removed from the model following LASSO procedures (i.e., 0 coefficients). The magnitude of estimates ranges from -0.1 (purple) to 0.1 (dark green), indicating the strength of the association with the cognitive outcome variable (see figure legend on right hand side), with gray cells representing retained model terms that were very small (non-zero) values. Coefficient names are structured such that the overall variable is listed first, followed by the level (for categorical variables) in square brackets (e.g., Smoking[Current]). R^2 values for each LASSO model: global cognition=0.118; memory=0.048; processing speed=0.129; executive function=0.202; reasoning=0.149.

FIGURE 2 LEGEND*.* Optimal time-use compositions for global cognition across the eight age/sex/BMI strata (listed on left-hand side of figure). The blue dots in the four left columns show optimal durations (in minutes, x-axis) of time-use behaviours (sleep, sedentary behaviour, light physical activity and moderate-vigorous physical activity, listed in the headers) for the 'average person' in each stratum. Supplementary Table 3 provides the values/levels of covariates used to define the 'average person' in each stratum. Gray dots represent the mean duration of each time-use behaviour observed in the respective strata (i.e., the average time-use composition for each stratum), whereas black dots represents the mean duration of each time-use behaviour for the overall sample (n=53,057). The right-most column shows the predicted global cognition z-scores for the compositions depicted on the left (e.g., blue dots in the right-hand column show the predicted global cognition z-score when each stratum achieves their optimal time-use composition, and gray dots in the right-hand column represent global cognition z-scores that correspond to current (observed) time-use compositions within the strata). BMI = body mass index, SB = sedentary behaviour, LPA = light physical activity, MVPA = moderate-to-vigorous physical activity, SD = standard deviation; 'w/ obesity' = with obesity; 'w/out obesity' = without obesity.

FIGURE 3 LEGEND. Optimal time-use compositions for cognitive variables (differentiated by colour) across age/sex/BMI strata (listed on right-hand side of figure). The coloured dots in the four left columns show optimal durations of time-use behaviours (sleep, sedentary behaviour, light physical activity and moderate-vigorous physical activity, listed in header) for the 'average person' in each of the strata. Supplementary Table 3 provides the values/levels of covariates used to define the 'average person' in each stratum. For example, moving from the left to right column, blue dots in the top row represent the optimal duration of sleep, sedentary behaviour, light physical activity and moderate-vigorous physical activity for processing speed performance, specifically for the female/aged <65 years/with obesity stratum. Gray dots represent the mean duration of each time-use behaviour observed in the respective strata, and black dots represent the mean duration of each time-use behaviour for the overall sample (n=53,057). The right-most column shows the predicted cognitive responses (z-scores) for the compositions depicted on the left (across optimised, stratum-averaged and whole sample-averaged time-use compositions). BMI = body mass index, SB = sedentary behaviour, LPA = light physical activity, MVPA = moderate-to-vigorous physical activity, SD = standard deviation; 'w/ obesity' = with obesity; 'w/out obesity' = without obesity.

FIGURE 4 LEGEND. Screenshot of the 'ideal day' interactive tool, which allows users to view their 'current day' (i.e., current 24-hr time-use composition) next to their 'best day' (i.e., optimised 24-hr time-use composition, personalised to their health and sociodemographic characteristics). Optimisation displayed in Figure 4 is based on a user with the following characteristics (i.e., inputs for tabs 3-5: sex=female; age=60 years; highest qualification=University/college; weight=80 kg; height=170 cm; high blood pressure=yes; smoking=current; alcohol consumption=≥3 standard drinks per week; type 2 diabetes=no; depression=no; social isolation=no; hearing difficulty or loss=no; traumatic brain injury=no; sleep=8.0 hrs, sedentary behaviour =13.0 hrs, LPA = 2.8 hrs; MVPA= 0.2 hrs.

FIGURE 5 LEGEND. Schematic diagram summarising the analytic workflow across four stages (data pre-processing, model selection, identifying 'optimal days' for cognitive performance, and creating the interactive tool using R Shiny). SB = sedentary behaviour; LPA = light physical activity; MVPA = moderate-to-vigorous physical activity; LASSO = Least Absolute Shrinkage and Selection Operator; BMI = body mass index.

FIGURE 6 LEGEND. Static representations (at two different viewing angles) of the 4-simplex tetrahedron containing all theoretically possible 24-hr time-use compositions with a random sub-sample (for viewability) of the female/aged <65 years/without obesity stratum. Each dot

represents one participant's 24-hour time-use composition. Dots that are closer to an apex (e.g., MVPA apex on the far left of the figure) represent greater time spent in that time-use behaviour. The 80th percentile ellipsoid fencing (transformed back to the compositional scale) is shown as a semi-transparent purple surface. Sampled time-use compositions are coloured orange if they are outside the fencing, and purple if they lie within the fencing. For the optimisation procedure, the model predictions on a grid of compositions (5-minute spacings) that strictly lie within the ellipsoid fencing (purple surface) are used to restrict possible time-use footprints to realistic values (i.e., time-use compositions represented by orange dots are not used in the optimal day predictions to ensure 'ideal days' are as realistic as possible for the stratum).