IOE, Faculty of Education and Society

Collecting saliva samples for DNA genotyping in a large-scale cohort study of young adults in England

CLS working paper number 2025/1

By Tugba Adali[1], Matt Brown[1], Alessandra Gaia[1], Morag Henderson[1], and Darina Peycheva[2, 3]

1 Centre for Longitudinal Studies, UCL Social Research Institute

2 Formerly, Centre for Longitudinal Studies, UCL Social Research Institute

3 UCL Institute of Epidemiology and Health Care

CENTRE FOR LONGITUDINAL STUDIES

UKRI Economic and Social Research Council

Contact the author

Tugba Adali

UCL Centre for Longitudinal Studies

t.adali@ucl.ac.uk

This working paper was first published in February 2025 by the UCL Centre for Longitudinal Studies.

UCL Social Research Institute

University College London

20 Bedford Way

London WC1H 0AL

www.cls.ucl.ac.uk

The UCL Centre for Longitudinal Studies (CLS) is an Economic and Social Research Council (ESRC) Resource Centre based at the UCL Social Research Institute, University College London. It is home to a unique series of UK national cohort studies.
For more information, visit www.cls.ucl.ac.uk.

This document is available in alternative formats. Please contact the Centre for Longitudinal Studies:
Email: clsdata@ucl.ac.uk

Contents

Disclaimer

This working paper has not been subject to peer review.

CLS working papers often represent preliminary work and are circulated to encourage discussion. Citation of such a paper should account for its provisional character. A revised version may be available directly from the author.

Any opinions expressed here are those of the author(s) and not those of the UCL Centre for Longitudinal Studies (CLS), the UCL Social Research Institute, University College London, or the Economic and Social Research Council.

How to cite this paper

Adali, T., Brown, M., Gaia, A., Henderson, M., and Peycheva, D. (2025) *Collecting saliva samples for DNA genotyping in a large-scale cohort study of young adults in England* CLS Working Paper 2025/1. London: UCL Centre for Longitudinal Studies.

Abstract

The collection of saliva samples in large scale social surveys is increasingly popular due to the possibility of obtaining DNA information to unlock research opportunities, and for their ease of administration in self-completion settings, in absence of trained nurses or interviewers. However, a number of methodological challenges in the collection of saliva samples remain unsolved. We analyse data from a cohort study of young adults in England: the Next Steps Age 32 survey to explore these methodological challenges. Approximately 57% of eligible cohort members consented to provide a saliva sample and 27% returned a sample to the laboratory, resulting in data for 24.7% of respondents being genotyped. Consent and sample return to the laboratory were associated with cohort members' characteristics (white ethnicity, being in a relationship, and better health) as well as survey-related characteristics (reading the saliva consent request booklet, participating in the prior survey wave, and consenting to linkage with health records). Furthermore, using experimental data we found that higher monetary incentives (£10 *vs*. £5) led to higher consent rates (57.8% *vs*. 53%) and a higher share of returned samples (29.8% *vs*. 20.6%). We also explore reasons for non-consenting, finding that most respondents motivate their decision with a vague answer (e.g. "don't want", "prefer not to", "no reasons"), while 26.9% mentioned they were uncomfortable with the task, found it intrusive, or expressed privacy concerns. We conclude with recommendations for survey practice. Our work contributes to an emerging body of research, destined to expand as the incorporation of biomarkers collection in mixed-modes large scale multi-purpose social surveys increases.

Keywords: Biological samples; Biomarkers; genetic data; return rates; Next Steps.

Acknowledgments: We are grateful for comments on an early version of this manuscript from David Bann, Tim Morris, and Richard Silverwood.

Introduction

In recent years, it has become increasingly common for large-scale social studies to collect biological samples from participants. This practice aims to enhance the understanding of the complex interplay between social, economic, and environmental factors and their impact on health outcomes. Examples of the types of biological samples collected include blood, urine, saliva, teeth, and hair. These samples are used to derive biomarkers and genetic information, providing valuable insights into various aspects of health. By integrating biological data with traditional survey data, researchers can explore a wide array of phenomena including investigating the relationships between social determinants and health, ultimately contributing to more comprehensive and effective public health interventions.

This study focuses on the collection of saliva samples for DNA extraction in an English cohort study. Saliva samples for DNA extraction have been collected in several multi-purpose large scale longitudinal and cross-sectional surveys, both in the UK and abroad. Examples include: the UK Biobank, the English Longitudinal Study of Ageing (ELSA), Next Steps, the National Child Development Study (NCDS), the Millennium Cohort Study (MCS), the National Longitudinal Study of Adolescent to Adult Health (Add Health), the Health and Retirement Study (HRS), the Future of Families and Child Wellbeing Study (FFCWS) (formerly known as the Fragile Families and Child Wellbeing Study), the Wisconsin Longitudinal Study, and the National Social Life, Health and Aging Project (NSHAP).

Adding genetic information to the data captured in social studies is particularly useful because it allows researchers to explore the genetic underpinnings of health and behaviour. By analysing genetic data alongside social and environmental factors, researchers can identify gene-environment interactions and understand how genetic predispositions may influence and be influenced by lifestyle, socioeconomic status, and other external factors.

DNA can be extracted from various types of biological sample but is most commonly extracted from blood or saliva. Compared to collecting blood samples, obtaining saliva samples offers several advantages. Saliva collection is less intrusive and burdensome for respondents and easier to administer, especially in certain population subgroups, such as children. Although saliva sampling kits are typically more expensive than

blood sampling kits, the overall cost is often lower due to savings on staff and DNA extraction expenses (Abraham et al., 2012). The ability to incorporate saliva sample collection in self-administered surveys is particularly promising, given the increasing use of web surveys and web-first mixed-mode studies in the social sciences. Finally, the quality of DNA extracted from saliva is comparable to that obtained from blood samples (Abraham et al., 2012; Bruinsma et al., 2018; Gudiseva et al., 2016), making it an attractive and minimally invasive approach (Hobcraft, 2007).

As more studies adopt the collection of saliva and other biological samples, it becomes increasingly important to understand the factors influencing respondents' willingness to both consent to providing a sample and then to return the collected sample to a laboratory. Identifying these factors is crucial not only for addressing obstacles to participation but also for assessing and correcting biases in consent and return rates.

In addition to participation rates, another critical aspect to evaluate is the usability of the samples returned to the laboratory. This includes determining how many samples are usable and identifying the main impediments to biomarker extraction, such as food contamination, incorrect labeling of kits, and empty kits. This information helps in forecasting sample sizes and identifying best practices for instructing sample members and survey staff (interviewers, laboratory staff, etc.) on how to provide, collect, and dispatch samples. Furthermore, sharing best practices on the logistics of collecting saliva samples, including feasibility and cost considerations, can enhance the efficiency of sample collection and the quality of the obtained samples. Standardizing protocols across studies through the sharing of best practices can also enhance comparability.

This paper describes the process of saliva sample collection in a mixed-mode cohort study of young adults in England: the Next Steps Age 32 survey. It reports on consent rates and return rates of saliva samples, respondents' characteristics associated with these rates, the effectiveness of monetary incentives, and respondents' stated reasons for non-consenting. The results of this study are particularly important given the increasing collection of biological data in social surveys (Calderwood et al., 2014) and the rise in the use of self-interviewing modes of data collection, such as web surveys. For a comprehensive overview of genomic data collected in several UK based cohort studies see Shireby et al. (2024) and Centre for Longitudinal Studies (2024).

Literature review

In the following we review the literature on the collection of saliva samples in large scale surveys. We focus on determinants of respondent willingness and factors which affect the successful collection and return of samples; the role of incentives in motivating respondents; and logistical and technical aspects that may lead to failure in the analysis of samples.

In order to genotype DNA extracted from saliva samples collected from participants in a social survey a number of steps must be completed successfully. First, sample members need to agree to participate in the survey. Second, they must consent to provide the sample. If the survey is administered in self-completion modes (e.g., postal or web), respondents must be provided with a collection kit (which will either need to be sent along with the survey invitation or sent later to those who consent). Third, participants then need to follow the instructions on how to collect the sample themselves and then finally they must return the sample to the study laboratory. The samples are then processed for DNA extraction, and only those with sufficient and uncontaminated material are successfully genotyped. There will inevitably be drop-off at each of these steps, with consequences not only in terms of statistical power for analysis, but also in terms of bias which may arise. For example, if respondents for which data are genotyped differ from those who are not genotyped in key variables of interest, there will be selection bias into the genotyped sample. This may happen for example if respondents with poorer health are less likely to participate in the task or less likely to return the sample.

We draw on the “conceptual model of factors influencing a respondent’s decision to provide a biomeasure” developed by Dykema and colleagues (2016). The authors describe three factors that influence provision of biological samples, i.e.:

1. Characteristics of the task – e.g. informed-consent processes, invasiveness, type of biomeasure sought, monetary incentives, measurement location (e.g. home or clinic) and person responsible for it (e.g. nurse, interviewer, self-administered).
2. Respondent characteristics – e.g. socio-demographics, cognitive ability, health, attitudes and beliefs).

3. Participation in the survey process (e.g. prior wave cooperation, willingness to comply with additional requests within the survey).

In the following sections we review the literature on each of these three aspects.

Task characteristics

Dykema et al. (2016) identify several dimensions related to task characteristics: "1) respondents' understanding of data-collection procedures, 2) methods for recruitment, 3) informed-consent language and processes (e.g., how measures will be used, such as for genetic testing), 4) the kind of biosample sought (e.g., saliva, blood), 5) the invasiveness of the method of measurement, 6) the setting for measurement (e.g., respondent's home, clinic), 7) who is responsible for taking the measurement (e.g., respondents themselves, respondents with assistance, another person), 8) the person's qualifications if the measurement is to be completed by another person (e.g., medical doctor, nurse, field interviewer), 9) and other survey-based characteristics (e.g., use of incentives)" (p. 59).

Regarding the collection of saliva samples, task characteristics vary depending on the biomarker of interest. For DNA genotyping, several studies – including Add Health, the Health and Retirement Study, the National Social Life, Health and Aging Project (NSHAP), the Wisconsin Longitudinal Study, and the Millennium Cohort Study – have used the Oragene© collection kit (Fitzsimons et al., 2022; Sakshaug et al., 2014). This method involves respondents spitting into a small container (which includes a preservative), sealing the sample with a cap, and returning it to a lab. An advantage of this protocol is its ease of administration in self-completion, without the need for nurses or trained interviewers, and the ability to collect samples in a home setting. These features help contain survey costs and minimize respondent burden, as participants do not need to travel to medical centres for sample collection, thus reducing the high drop-off rates typical of follow-up nurse or clinic visits administered after survey interviews (Clemens, Given, and Purdon, 2012, as reported in Calderwood et al., 2014).

Collection of saliva sample for reasons other than DNA genotyping (e.g. cortisol measurement) can involve protocols that are more burdensome[1]. Clearly, the complexity of the task influences respondents' ability to understand the process, the feasibility of self-administration, and the level of burden on respondents.

Studies also vary in how informed consent is collected, with protocols depending on the range and type of sample required. In some studies, consent for the collection of biomeasures or specimens is collected in a written form signed by the respondent (Avendano, Scherpenzeel, and Mackenbach, 2018; Etter, Perneger, and Ronchi, 1998; O'Doherty et al., 2021). As noted by Avendano, Scherpenzeel, and Mackenbach (2018), a significant obstacle to participation in the collection of saliva samples in the Longitudinal Internet studies for the Social Sciences (LISS) panel was the return of consent forms, with about 50% of participants who initially agreed to participate not returning the signed forms. It is unclear whether these respondents changed their minds or were unwilling to admit their intention not to participate, or if they were willing but failed to comply with the additional burden of signing and returning the forms. While this study collected saliva samples to measure cortisol, we expect similar barriers to apply for saliva samples collected for genetic analysis.

Finally, survey-based characteristics, such as monetary incentives, may influence respondents' willingness to provide a saliva sample and return it to the lab. Incentives may be linked solely to survey participation or have two components: one for survey participation and one for providing the biological sample(s). The literature on the effectiveness of monetary incentives for collecting biological samples in social surveys is limited (Avendano, Scherpenzeel, and Mackenbach, 2018).

Beyond monetary incentives, additional strategies to motivate study participants to consent to biomarker collection include offering feedback on test results. While providing feedback on DNA is generally unfeasible in the context of a social survey, this practice is more straightforward for other types of biomarker. Experimental research (Benzeval et al., 2023) has demonstrated that sharing blood test results with

[1] For example, in the English Longitudinal Study of Ageing (ELSA), respondents are asked to collect samples four times throughout the day at specific moments (i.e., at wake-up, half an hour after wake-up, at 7 PM, and at bedtime). This process involves chewing on a plastic-coated cotton swab until saturated, packing the samples, mailing them back, and completing a complementary survey covering various aspects, including the respondent's mood at each sample collection time. A similar approach was adopted in a pilot study within the LISS panel, where measurements were taken five times a day to measure the cortisol rhythm over the day (Scherpenzeel and Bottenheft, 2024).

participants can positively impact their willingness to consent to sample collection. Nonetheless, ethical, logistical, and methodological challenges should be considered (see discussion section).

Respondents' characteristics associated with consent and return rates, and usability of samples

According to the framework developed by Dykema et al. (2016), respondent characteristics influencing the likelihood of providing a biological sample include socio-demographic characteristics, cognitive ability, health status, and attitudes or beliefs. Findings from large-scale studies analysing socio-demographic differences in the propensity to provide a saliva sample for DNA genotyping are mixed and, in some cases, not easily generalizable due to the specificity of the study populations and data collection protocols (e.g., mode of data collection, incentives, number of other biosamples collected, or other survey tasks).

For example, Dykema et al. (2016) found that the likelihood of providing a saliva sample was lower among females, individuals with lower education and cognitive ability, those who were socially isolated, in poorer health, had less contact with the healthcare system, and were more religious. However, these results are based on the Wisconsin Longitudinal Study (WLS), which is relatively homogeneous in terms of age, education, and ethnicity (predominantly white), as it follows respondents who graduated from Wisconsin high schools in 1957. At the time of saliva DNA collection, participants were in their late 60s, the saliva collection was self-administered, samples returned by mail, and a $5 incentive was offered.

Another U.S.-based study of older adults aged 51 years or older (the 2006 Health and Retirement Study) investigated the association between socio-demographic factors and consent to three sets of physical measures (i.e., body measurements, saliva sample for DNA extraction, and blood spot samples) (Sakshaug, Couper, and Ofstedal, 2010). The odds of consenting to all physical measurements slightly decreased with age. In terms of ethnicity, Hispanics were more likely to consent than non-Hispanics, while this study does not find differences for black or "other" ethnicity compared to the white reference group. Additionally, the interaction between sex and ethnicity showed that black women were more likely to consent compared to black

men. Respondents living with one or more other eligible persons were more likely to consent. Regarding other demographics, no differences were found with respect to gender, educational level, or attendance at religious services. Consent was not significantly associated with self-reported health, body mass index, *Medicare* status, pain, or diagnosis of several diseases although diabetics were more likely to consent than non-diabetics. Respondents who rarely engaged in even light physical activities were less likely to agree compared to more active individuals. Additionally, participants with more functional limitations had lower odds of consenting. Respondents who had visited a doctor within the past two years were generally more willing to consent. However, the relationship between doctor visits and participants' perception of their health did not significantly influence their decision to participate.

In the Age 14 Sweep of the Millennium Cohort Study (Age 14), young people and their resident biological parents were asked to provide saliva samples for DNA extraction. The study offered no monetary incentives (either for participation in the survey or the provision of samples). Consistent with Dykema et al. (2016), educational level (household highest educational qualification) was significantly associated with a higher likelihood of providing a sample for cohort members, mothers, and fathers. Other main findings indicated a lower likelihood of sample provision among ethnic minorities (for cohort members, mothers, fathers, and "triads," i.e., cohort members, mothers, and fathers).

Finally, results from the U.S.-based National Health and Nutrition Examination Survey (NHANES) show that the likelihood of consent for genetic analysis was lower for women (versus men) and non-Hispanic blacks (versus non-Hispanic whites) (McQuillan, Pan, and Porter, 2006). Conversely, no differences were observed with respect to education and poverty level. Additionally, middle-aged participants were less likely to agree to provide samples than younger and older age groups.

Survey process characteristics

Survey process factors identified by Dykema and colleagues include resistance to survey participation (within the wave in which the biomedical sample is collected), participation in additional survey tasks (within that wave), and prior wave participation.

When these factors are tested empirically (operationalized as incomplete prior participation, number of call attempts, and prior wave refusal), they all prove to be negatively associated with consent to provide a saliva sample (Dykema et al., 2016). This is consistent with results from the Health and Retirement Study (Sakshaug, Couper, and Ofstedal, 2010), which models the association between measures of resistance to the survey interview and consent to three biological measures, including saliva samples for genotyping. The authors find that consenters required fewer contact attempts to reach cooperation both in the current and prior waves, showed fewer signs of impatience and need for confidentiality reassurances during the interview, and had higher ratings on cooperativeness and interview enjoyment. However, neither the mode of data collection at the prior wave (telephone versus face-to-face) nor the time elapsed since the last interview were correlated with consent.

Research questions and hypotheses

This paper describes the process of saliva sample collection in a mixed-mode wave of a longitudinal cohort study of young adults in England: the Next Steps Age 32 survey. Furthermore, we answer the following research questions:

1. What were the consent rates to provide a saliva sample and what were the return rates? Among returned samples, how many were of sufficient quality to allow DNA extraction and genotyping?
2. What were the respondents' characteristics (i.e. socio-demographic, health and personality traits) and survey process characteristics (e.g. prior survey participation and data collection mode, *etc.*) associated with consent rates and return rates?
3. Were monetary incentives effective in boosting return rates?
4. What were the reasons for non-consenting?

With reference to research question 1, there was uncertainty on predicted consent and return rates, given that this was the first time Next Steps participants were invited to provide a biological sample (or any biomeasure) and the available literature was not adequate to provide robust forecasts for this specific cohort (32 years old in the UK).

Possible reference figures for comparison are available from another UK-based cohort: the Millennium Cohort Study (MCS). In the pilot study to the Millennium Cohort

Study, age 11 saliva samples were obtained from 73% of mothers, 76% of fathers and 74% of children. However, this pilot study was based on a small sample of only 45 families, in 5 areas of the UK (Calderwood et al. 2014). At age 14 of the Millennium Cohort Study, 81.4% of eligible cohort members provided a sample, and DNA was successfully extracted for 78.4% of those eligible (Fitzsimons et al. 2022). However, consent and return rates between the two studies may differ due to fundamental differences between these age groups, study characteristics and survey climate changes between the two fieldwork periods 2015-16 (for MCS Age 14) and 2022-23 (for Next Steps). For instance, 32-year-olds decide autonomously on consent and may face additional barriers to returning the sample, such as competing demands from work and family responsibilities. These issues are less relevant for children and adolescents whose participation might be guided or supported by parents or caregivers.

With respect to research question 2, based on evidence from the literature we explore the impact on consent and return rates of the following socio-demographic factors (gender, ethnicity, social class, educational attainment, cohabitation status, self-assessed general health, personality traits, and generalised level of trust in others) and survey characteristics (prior wave participation, mode of participation in the current wave, data linkage consent, and self-reported consultation of the saliva collection booklet).

With respect to gender differences, in line with prior research, we hypothesised that (conditional on survey participation) males would have higher propensities to consent and return the sample. With respect to ethnicity, we hypothesised that ethnic minorities would have a lower likelihood of consenting to saliva collection and returning the sample to the lab. This hypothesis is consistent with most of the literature and especially with evidence from the Millennium Cohort Study, which (like Next Steps) is also a UK-based cohort study.

With regards to education, we expected highly educated individuals to have a higher propensity to consent and return the sample. In terms of the association between socio-economic status and compliance with the saliva collection task, we did not hold specific hypotheses.

In terms of the association between health and consent and return rates of the saliva sample, our hypotheses were mixed. On the one hand, theoretically, we would expect topic salience to motivate respondents, and hence poor health to be positively associated with consent to saliva sample collection and return of samples to the lab. On the other hand, prior research on older cohorts (Dykema et al. 2016) shows a lower participation to saliva collection amongst individuals in poor health.

In terms of attitudes and personality traits, we hypothesised that participants with higher levels of trust, who are more open to new experiences, score higher in conscientiousness scales (which includes measures of being disciplined, responsible and well organised) and also those who are classified as having higher levels of agreeableness would be more likely to both consent and return samples. Conversely, we have a mild expectation that extraversion might be positively associated with consenting and returning samples as this trait may be a proxy for social integration, and prior research shows that individuals who are more socially isolated tend to be less likely to be willing to provide samples (Dykema et al. 2016).

With respect to factors that are related to the survey experience, our hypothesis is that cohort members who are more cooperative (e.g. that participated in the prior survey wave) will be more likely to provide a saliva sample. In a similar vein, we also expect higher compliance with the saliva protocol from cohort members who consented to the linkage of survey data with health records. This might be partly because consenting to data linkage may signal a greater commitment to the survey and partly because those willing to link their health records may consider health-related research to be more valuable.

Our hypothesis is that reading the saliva collection booklet would increase the chances of both consenting to provide a saliva sample and returning the sample to the lab. On one hand, the information included in the booklet may address respondents' concerns but on the other hand respondents who are more inclined to consent and more committed to the study are also more likely to read the survey accompanying materials.

Finally, we do not have a specific hypothesis regarding how the mode of data collection may influence consent to provide a saliva sample. Interviewers play an essential role in helping respondents understand the process, addressing any concerns, and

ensuring the sample is returned to the lab. On the other hand, respondents who participate in the face-to-face phase of fieldwork are those who did not complete the survey online within the first three weeks, suggesting they may, on average, be less committed to the study. Therefore, it remains unclear whether the positive effect of interviewer presence or the negative effect of self-selection will dominate.

While this paper focuses on saliva samples, many of the considerations presented here are valid also for other types of biological samples (e.g. blood) routinely collected by several large-scale cross sectional and longitudinal studies.

Data and Methods

The Next Steps Study and the Age 32 Survey

Next Steps, previously known as the Longitudinal Study of Young People in England (LSYPE), began in 2004 and included young people in Year 9 who attended state and independent schools in England. Following the first wave, when participants were aged 13-14, study members were interviewed annually for a total of seven waves until they were aged 19-20, mapping their journeys from compulsory schooling to university, training, and entry into the labour market. The study was initially funded and managed by the Department for Education (formerly known as the Department for Education and Skills), the government department responsible for children's services and education in England. At each wave, study members who participated in the previous sweep were invited to take part. In 2013, the study was transferred to the Centre for Longitudinal Studies (CLS) at UCL, and since then the scope of the study was broadened to cover all aspects of study members' lives. The first survey after this transition was the Age 25 Wave (Wave 8), conducted in 2015/2016, where all study members who had ever participated were invited, except those who had withdrawn, passed away, or were in prison or probation.

The most recent wave, the Age 32 survey, was conducted between April 2022 and September 2023. This wave focused on early adulthood, with questions on work and careers, education and training, housing, partnerships, children, health, mental health and wellbeing, and attitudes. It also sought consent to link data from health records, economic records and other administrative data sources. Additional survey requests included a cognitive assessment measuring working memory and the collection of

saliva samples for DNA extraction for genetic research. The study obtained ethical approval from the NHS Research Ethics Committee (REC Reference 22/EE/0052), and the fieldwork was conducted by Ipsos. More information on the study content is available in the cohort profile, see: Wu et al. (2024).

A total of 13,859 study members were issued for fieldwork in the Age 32 survey, divided into five batches for management purposes: a “soft launch” involving a random quarter of the sample, followed by three more batches (Batches 1, 2, and 3), and a separate online-only batch (Batch 4) issued simultaneously with Batch 3. A total of 7,279 study members participated in this wave, resulting in a response rate of 53%, calculated according to RR2 as set by the American Association for Public Opinion Research (AAPOR) guidelines (AAPOR 2023).

The first four waves of Next Steps were conducted face-to-face, but from Wave 5 onwards, a sequential mixed-mode approach was adopted, in which participants were first invited to take part online, with non-respondents being followed up by telephone then by face-to-face interviewers. In the Age 32 survey, all study members were initially invited to participate online. After a three-week online-only period, interviewers began following up face-to-face. During this stage, the online survey remained open, and interviewers could also offer additional modes including video interviewing (via MS Teams), temporarily providing a tablet/secondary device for self-completion, and telephone interviewing. When interviewers had exhausted all contact attempts, non-respondents were invited to participate in an abbreviated non-response conversion online survey (mop-up survey). An experiment during the soft launch compared the effectiveness of an abbreviated (20 minute) mop-up survey versus asking participants to complete the full (60 minute) survey. A significantly higher response rate was obtained for cohort members allocated to the shorter online survey (Gaia et al., 2024a); hence, non-respondents in Batches 1 to 4 were offered this version which did not include the request for saliva sample collection. Overall, 86% of all interviews were conducted via web, 10% in-home with an interviewer, 2% via telephone, 2% via secondary devices, and less than 1% via video interviewing.

All participants were offered monetary incentives in the form of vouchers. During the soft launch phase, an experiment was conducted to evaluate whether differential incentives (targeted at prior wave non-respondents) would improve response rates. In the differential incentive experimental group, cohort members who were non-

respondents at the prior wave were offered £25 conditional on survey completion, while those who participated in the prior wave were offered a £15 conditional incentive. In the control group, all cohort members were offered a £20 conditional incentive. Additionally, all cohort members were offered a £10 incentive for completing the online survey within the first three weeks of fieldwork. The differential incentives design did not improve response rates (Gaia et al., 2024b); hence, the flat incentive strategy was retained for the remaining waves – i.e., all cohort members were offered a £20 conditional incentive and an additional £10 incentive for completing the online survey within the first three weeks. Participants were offered an additional incentive for returning the saliva sample. During the soft launch the incentive was £5, which was subsequently increased to £10 for the remaining batches of fieldwork.

The data used to answer our research questions are data and *paradata*[2] from the Next Steps Age 32 Survey; additionally, data has been supplemented with survey variables from the previous waves (University College London, UCL Institute of Education and Centre for Longitudinal Studies 2024).

Saliva sample collection protocol in the Next Steps Age 32 Survey

The request to provide a saliva sample in the Age 32 survey was the first time that Next Steps participants had been asked to provide any form of biological sample. Prior to the Age 25 Survey, the study had primarily focused on education and the transition to the labour force, with less emphasis on physical and mental health. These topics gained prominence starting from the Age 25 Survey. Other longitudinal studies in Britain (e.g. 1958 National Child Development Study, 1970 British Cohort Study) have a long history of conducting medical assessments and collecting objective measures of health (such as weight, blood pressure etc) but Next Steps has never previously included any such measures. The request for a saliva sample for DNA extraction therefore marked a significant development for the study, and there was uncertainty as to how this request would be received by participants. Therefore, significant care was required in designing the protocol to highlight the benefits and scientific importance of collecting the sample, maximize informed consent, address privacy and

[2] *Paradata* are available upon request via the Centre for Longitudinal Studies (University College London) Data Access Committee.

confidentiality concerns, and manage the additional response burden associated with the collection and return of samples.

An additional challenge was motivating respondents in self-administered modes (i.e., the online component of the web-first mixed-mode design). These respondents were first invited to consent and then to self-collect and post their samples to a lab.

The following protocol was used to collect the samples. First, along with advance materials sent as part of the survey invite, cohort members received a separate, 4-page A5 booklet explaining the relevance of genetic information for health research and the motivation for its collection within the Next Steps study. The booklet also contained information on what DNA extraction entails, how DNA would be accessed and stored, whether study members could expect any feedback, and information on withdrawing their consent. The booklet emphasized the offer of a monetary incentive: cohort members were informed that they would receive a voucher if their sample was received in the lab, and that the incentive for providing the saliva sample was completely independent of the main survey incentive (which was conditional on completing the survey questionnaire). The information provided in the booklet was also covered on the respondent website[3]. The booklet is available in the supplementary materials.

The saliva consent request was placed towards the end of the questionnaire[4]. In this section, a brief introduction informed study members that a saliva collection kit would be sent to their address should they agree to provide a sample. Cohort members were also informed that the collection kit would include a prepaid return jiffy bag to return the sample to the lab and were reminded of the incentive. They were then asked if they had read the booklet mentioned above, and if not, were provided with a list of Frequently Asked Questions (FAQs) covering the information included in the booklet. In self-administered modes, cohort members were asked to read the FAQs, while in interviewer-administered modes, interviewers would read the FAQs to respondents. The consent question itself included bullet points summarizing what study members were agreeing to by consenting. Study members who did not consent to providing a sample were asked an open-ended question to understand the reasons or concerns

[3] The Age 32 FAQs page is available here: https://nextstepsstudy.org.uk/home/surveys/age-32-survey/
[4] The questionnaire for the full survey is available here: https://cls.ucl.ac.uk/cls-studies/next-steps/next-steps-age-32-sweep/

behind their choice. Consent was recorded electronically with the questionnaire script – i.e. there was no paper consent form.

In all modes except for in home-interviewing, Oragene DNA OG-500 saliva collection kits were then shipped to study members who consented to providing a sample, along with another booklet explaining how to provide the saliva sample, a plastic specimen bag to place the saliva tube in for return with absorbent material inside, a serial number label sheet (cryogenic labels to attach to tube and bag), and a white “exempt human specimens” jiffy bag for return (with prepaid postage). There was also a cover letter which included a link to a video that explained the process of self-collecting the saliva sample using the kit.

During in-home interviews, the interviewers supplied the kits and asked participants to collect the sample there and then so that they could post it to the lab on the study members’ behalf. However, if for any reason study members were not able to supply a sample at the time, they were given the option to post the samples back later.

The instructions provided to study members explained how to take the tube out of packaging, how to fill it with the amount of saliva required, seal the tube, place a barcode on the tube, package it and ship it. Cohort members were asked to: i) refrain from eating, drinking, smoking or chewing gum 30 minutes before providing the sample to ensure the sample’s quality; ii) ship the sample as soon as possible after collection, and iii) store it at room temperature away from direct light until shipment.

Samples were received by the Bristol Bioresource Laboratories (BBL), University of Bristol, for DNA extraction, in a lab licensed by the Human Tissue Authority. Version 3 of Illumina’s Global Screening array (GSAv3) was used as the genotyping array. The lab did not have any access to study members’ personal information nor survey responses.

Improvements to the saliva collection protocols

The Age 32 Survey was conducted in batches. The first batch was regarded as a Soft-launch and was used as a final test of all survey procedures. A random sub-sample

(n=3,113) of the total sample (n=13,859) were issued to the soft-launch[5][6]. The protocols described in the previous section apply to the entire study. However, following the soft launch phase, some changes were made to attempt to increase consent and return rates before the remaining batches were issued to field.

First, the incentive offered for return of the saliva sample was increased from £5 to £10. The incentive offer was also made more prominent on the booklet cover.

Second, the wording of the saliva collection booklet, along with the FAQs on the respondent website and in the questionnaire script, was slightly revised. These updates incorporated information gathered from an open-ended question addressing reasons for non-consent. Based on this feedback, the updated materials further emphasized the importance of collecting the saliva samples, the intended use of the DNA samples, and made additional reassurances regarding who would have access to the data and how it would be securely managed.

Finally, the mailing of the voucher for survey completion was slightly delayed to increase the likelihood that participants would receive their saliva collection kits before they received their main survey incentive. This adjustment addressed concerns that receiving the higher value voucher for survey participation first could reduce the impact of the offer of an additional £10 incentive for returning the saliva sample.

These amendments allow us to assess the combined effect of the increase in the saliva conditional incentive (from £5 to £10) and the other minor changes in the protocol on consent and return rates.

[5] Towards the end of fieldwork, a fourth batch was issued to field. This batch (n=769) is considerably smaller in size compared to other batches and consisted of cohort members who weren't initially issued to the field. Most of these cases were considered permanently untraced; they were however later invited via post after their addresses being traced by NHS Digital. The saliva sample collection procedures implemented for batch 4 were identical to those of batches 1 through 3. These cases are excluded from the analysis on the effectiveness of incentives for saliva collection, as they were not randomly allocated to any of the initially issued batches (i.e. soft-launch and batches 1-3).

[6] Soft-launch cohort members who participated in the non-response survey via the full data collection instrument are excluded from the analysis, for comparability with batch 1 to 3 participants to the non-response survey, who were not invited to provide a saliva sample. For more information on the non-response survey see Gaia et al. (2024b).

Methods

To answer research question 1, we summarize the consent and sample return rates for saliva sample collection, as well as the rates of DNA extraction and genotyping.

Research question 2 is addressed using three logistic regression models which explore the determinants of consent and sample return. The dependent variable for Model 1 is a dichotomous variable indicating whether the respondent consented to provide a saliva sample (1 = consented, 0 = did not consent). The dependent variable for Models 2 and 3 is a dichotomous variable indicating whether the respondent returned the saliva sample to the lab (1 = returned, 0 = did not return). The analysis sample for Model 2 is composed of all eligible cohort members, while the analysis sample for Model 3 includes cohort members who consented to provide the saliva sample. The independent variables include respondent characteristics (gender, ethnicity, social class as measured by NS-SEC, educational attainment, cohabitation status, self-assessed general health, subscales of the Big Five personality traits, and generalised level of trust in others[7]) and survey behavior variables (participation in the Age 25 wave, mode of participation in the Age 32 wave, whether they reported reading the saliva sample collection booklet[8], and consent to data linkage from health records).

To assess the effectiveness of increased monetary incentives (research question 3), we compare the saliva sample consent and return rates from the soft launch with those from batches 1-3 of fieldwork using chi-square tests.

Finally, to answer research question 4, we analyse study participants' reasons for not providing consent. This information was collected through an open-ended question and coded by the fieldwork agency Ipsos into 26 categories, which we further recoded into broader categories for meaningful analysis (see results section for more details).

[7] These variables are measured at the Age 32 wave.
[8] Participants were asked whether they have read the leaflet. Those reporting not having read the leaflet were provided with information from the leaflet in the survey script.

Results

RQ1: Consent and return rates and quality of the samples

Of the 7,329 cohort members who took part in the Age 32 survey, 6,352 were asked for consent to provide a saliva sample. Of those asked, 57% agreed to provide the sample, and 27% returned it (Table 1). The return rate amongst consenters was 48% (not shown in table).

Upon receipt at the lab, some of the saliva samples could not be used. Some kits were found to be unused or had leaked, some respondents withdrew consent between the survey completion date and the sample being received and processed by the lab, and 302 cases were lost due to technical issues. This resulted in 1,717 saliva samples from which DNA was successfully extracted. However, not all saliva samples could be matched to study member IDs, resulting in DNA being available for genotyping for 1,698 cohort members, which constitutes 26.7% of those invited to provide a saliva sample.

In 15 cases, DNA concentration was insufficient to proceed with the genotyping, reducing the sample to 1,683 cases. Quality control checks on the genotype data resulted in the removal of data for 115 cases meaning that the final dataset includes data for 1,568 cases, corresponding to 25% of those invited to provide a sample. Quality controlled genotype data was derived from 89% of all samples received at the laboratory. Please see Centre for Longitudinal Studies (2024) for details on the CLS led data quality checks.

Table 1. Saliva sample consent and return rates, DNA extraction and successful genotyping

Consent, return rates, DNA extraction and genotyping	N	%
Consent to saliva extraction	3,591	56.5%
Saliva kit sent back to the lab (as recorded by the lab)	1,766	27.8%
Saliva sample sent back to the lab and linked to study member	1,733	27.3%
DNA extracted	1,717	27.0%
DNA suitable for genotyping	1,698	26.7%
DNA genotyped	1,683	26.5%
Genotyping passed quality control	1,568	24.7%
N	6,352	100.0%

Note: The final row indicates the number of cohort members invited to provide a saliva sample.

Table 2 shows the DNA concentration in the genotyped samples (before data quality checks at CLS). The table includes cases with a low concentration which were treated and successfully genotyped (<5.5ng/ul) while it excludes cases which had the lowest concentration which could not be genotyped. The majority of these saliva samples had a DNA concentration which allowed DNA extraction, the minimum DNA concentration (as ng/ul) was 0.28, and the largest was 628.51 (mean=90.11).

Table 2. Distribution of genotyped cases by DNA concentration range (ng/ul)

DNA concentration	Number	%
Conc. >50 ng/ul	1,075	63.9%
38.5< Conc.<50	149	8.9%
5.5< Conc.<38.5	434	25.8%
Conc.<5.5	25	1.5%
Total genotyped	1,683	100.0%

RQ2: Characteristics associated with consent and return rates

Table 3 shows the association between consent and return rates and respondents' and survey design characteristics. The outcome variables were: consent (Model 1) and return of sample (Model 2 and 3). Model 2 was run amongst all those invited to provide a sample while Model 3 analysed return of sample amongst consenters.

Gender was not a significant predictor of consent nor returning a sample but participants of white ethnicity had far higher of odds of consenting to saliva collection (OR: 1.807, P<0.001) and returning the sample (O.R.:1.652, P<0.001, among eligible sample members and O.R.: 1.207, P=0.036 among consenters).

Contrary to our expectation, neither social class or education level were associated with consent or sample return rates. Conversely, having a cohabiting partner slightly increased the odds of returning a sample among all eligible respondents. However, the effect is relatively small (O.R.=1.144, P=0.042) and little difference based on relationship status was found in consenting to provide a saliva sample or on returning the sample conditional on having given consent.

With respect to health, study members who reported better general health compared to the reference group (poor) all showed lower odds of consenting to providing a saliva sample. This result is consistent with the hypothesis that topic salience is associated with higher level of consent to participate in the saliva sample protocol, i.e. those experiencing health problems may have a stronger drive to support health research. However, when we analysed the probability of returning the saliva sample after having consented, those with the highest self-reported health ("excellent") have the higher odds of returning the saliva sample (O.R.=1.496, p=0.045) as opposed to their peers reporting poor health. This latter result seems to suggest that, with respect to returning the sample, the standard non-response theory – which suggests that physical and mental health issues may incapacitate the respondent to participate in surveys (Groves and Couper 2012)– is more likely to apply as opposed to topic salience. All other health levels were not associated with a propensity to return the sample that differs from respondents in poor health.

Those with higher levels of trust in other people were not significantly more likely to consent but trust seemed to be important at the sample return stage. Compared with

sample members reporting a higher level of trust, those reporting a lower or medium level of trust had lower odds of returning the samples (respectively, OR: 0.817, P=0.013 and OR: 0.743, P<0.001). This is consistent with our hypothesis that higher trust would motivate adherence to the protocol.

In terms of psychological traits, findings were mixed. Consistent with our expectations, the agreeableness subscale – which measures a person's tendency to be cooperative, compliant and trusting towards others – was positively associated with higher consent to provide a saliva sample (OR=1.028, P=0.046), but not significantly associated with returning the sample.

We do not find support for our hypothesis that openness to new experiences would be associated with higher consent, or that conscientiousness (capturing organisation, discipline and sense of responsibility) would be associated with higher return rates. Neither scales were significantly associated with consent or return rates.

Contrary to our hypothesis, extraversion – which we viewed as a potential proxy for being socially integrated – was not significantly associated with consent to provide a sample, but was associated with *lower* propensity to return the sample (i.e. O.R. 0.962, P=0.002 and O.R.=0.958, P=0.004, respectively for return rates among all eligible sample members and among consenters).

Somewhat unexpectedly, cohort members scoring higher on the neuroticism scale – measuring how people experience and react to negative emotions and stressful situations – showed a slightly higher propensity to return the sample once they consented (O.R.=1.037, P=0.012). However, it is unclear which mechanism (if any) is driving this result.

When exploring whether cohort member engagement with the survey was associated with compliance with the saliva sample collection protocol we found interesting results. First, as expected, sample members that participated in the prior survey wave, i.e. the Age 25 survey, had higher odds of returning the saliva samples (both overall, O.R.=1.346, P<0.001, as well as among consenters, O.R.=1.537, P<0.001), although prior wave participation was not predictive of higher odds of consenting. As one might expect, having read the saliva collection leaflet is significantly and very strongly correlated with both the decision to consent to provide a saliva sample (OR=3.481,

P<0.001) and to return the sample to the lab (among all eligible participants OR:3.117, P<0.001, among consenters OR=1.815, P<0.001).

Also, the odds of consenting to the saliva sample collection are five times higher for respondents who over the life of the study have agreed to linkages of their survey data with health records compared to those who did not consent to data linkage (OR=5.091, P<0.001) and the odds of returning the sample (among those willing to participate in the saliva collection) are almost twice as high for data linkage consenters (*versus* non-consenters) (OR=1.655, P<0.001). In this context, it should be noted that linkage with health records refers specifically to data held by the National Health Service (NHS England). This includes primary care records from visits to family doctors and other health professionals, as well as Hospital Episode Statistics (HES), which cover hospital admissions and attendances, for further information see: Ipsos (2024).

In interpreting the role of mode of data collection on saliva sample collection one should note that face-to-face respondents are participants who did not participate in the first weeks for the fieldwork period, when the survey was administered solely by web. Hence, these cohort members are on average less engaged or compliant with the study. Not surprisingly, therefore, participants who completed the interview in the presence of an interviewer have lower odds to consent to provide a saliva sample. As cohort members self-select into modes, we interpret this result as being driven by selection effects: less engaged or compliant cohort members are more likely to participate in the survey after the web fieldwork period.

However, once a cohort member has agreed to provide a saliva sample, interviewers play an important role in ensuring that the sample is returned to the lab. Indeed, the odds of returning the sample were higher in the interviewer administered modes as opposed to other modes (O.R.=1.548, P<0.001). We also found a strong and positive correlation between sample returns (among consenters) and the responsibility of returning the sample being with face-to-face interviewers. The odds of returning the sample are approximately 16 times higher in face-to-face interviews *versus* online, telephone, video and secondary devices interviews (results not shown).

Table 3. Logistic regressions predicting consent and return rates

	(1) Consent		(2) Return (amongst eligible)		(3) Return (amongst consenters)	
Respondent characteristics	OR	*p*	OR	*p*	OR	*p*
Gender (Ref=male)						
Female	1.084	*0.187*	1.002	*0.979*	0.951	*0.499*
Not binary or other	0.992	*0.981*	1.757	*0.097*	2.123	*0.076*
White ethnic background	1.807	*<0.001*	1.652	*<0.001*	1.207	*0.036*
NS-SEC (Ref=semi-routine, routine, never worked or long-term unemployed)						
Managerial, administrative and professional occupations	1.136	*0.170*	1.088	*0.396*	1.043	*0.708*
Intermediate, lower supervisory and technical occupations, small employers and own account workers	1.079	*0.441*	1.075	*0.496*	1.066	*0.598*
Achieved first degree or higher	0.918	*0.188*	1.060	*0.399*	1.125	*0.137*
In a cohabiting relationship	1.104	*0.109*	1.144	*0.042*	1.095	*0.226*
Self rated health (Ref=poor)						
Excellent	0.480	*<0.001*	0.987	*0.943*	1.496	*0.045*
Very good	0.467	*<0.001*	0.864	*0.391*	1.312	*0.144*
Good	0.462	*<0.001*	0.764	*0.113*	1.108	*0.576*
Fair	0.535	*<0.001*	0.841	*0.339*	1.131	*0.531*
Trust (Ref=high)						
Low	0.866	*0.062*	0.817	*0.013*	0.835	*0.056*
Medium	0.895	*0.103*	0.743	*<0.001*	0.728	*<0.001*
Agreeableness Subscale	1.028	*0.046*	1.011	*0.475*	0.994	*0.708*
Openness Subscale	1.001	*0.894*	0.995	*0.546*	0.991	*0.390*
Conscientiousness Subscale	0.993	*0.584*	1.006	*0.682*	1.014	*0.383*
Extraversion Subscale	0.986	*0.243*	0.962	*0.002*	0.958	*0.004*
Neuroticism Subscale	0.988	*0.294*	1.019	*0.131*	1.037	*0.012*
Survey related variables						
Productive in Age 25 wave	0.902	*0.169*	1.346	*<0.001*	1.537	*<0.001*
Consented to linkage with health records	5.091	*<0.001*	4.071	*<0.001*	1.655	*<0.001*
Read the saliva booklet (Ref=no)						
Yes	3.481	*<0.001*	3.117	*<0.001*	1.815	*<0.001*
Did not received the booklet	2.133	*<0.001*	1.695	*<0.001*	1.125	*0.288*
Interviewer-administered mode (i.e. in home, video, telephone)	0.712	*<0.001*	1.184	*0.072*	1.548	*<0.001*
Constant	0.283	*<0.001*	0.039	*<0.001*	0.212	*<0.001*
N	*6,216*		*6,216*		*3,557*	

Note: The regression models were conducted using complete case analysis for the outcome variable and numeric independent variables (i.e. the personality subscales), where cases with missing data were excluded. For categorical independent variables, missing data were retained as separate categories but are not reported in the table.

RQ3: The effect of incentives on saliva sample collection

Table 4 shows that the increase in the incentive amount from £5 to £10 (along with some changes in the communication strategy) resulted in a 5 percentage point increase in consent rates, from 53.0% to 57.9%. Differences are more pronounced for sample return rates, which is the stage that determines whether study members qualify for the incentive as study members who consent to the saliva request but do not provide the sample are not eligible for the incentive.

Among all eligible study members, the level of sample return increased by from 20.6% to 29.8%. Among all who consented, the level of return was 38.9% before the change in the incentive amount and over a half (51.5%) afterwards. All differences are tested using Chi-square tests and are highly significant. We thus confirm our hypothesis of a positive effect of monetary incentives on saliva sample consent and return rates.

Table 4. Rates of consent and return by experimental group

Rates of consent and return by experimental group

	Lower incentive group	Higher incentive group	Total	P-value
Consent	53.0%	57.9%	56.6%	0.001
N	*1,563*	*4,693*	*6,256*	
Return (all)	20.6%	29.8%	27.5%	<0.001
N	*1,563*	*4,693*	*6,256*	
Return (consenter)	38.9%	51.5%	48.6%	<0.001
N	*828*	*2,715*	*3,543*	

Note: Excludes “long” mop-up completions, as well as Batch 4 participants. P-value from Pearson Chi-Square

RQ4: Reasons for not consenting to provide a sample

Item non-response was very high on the question regarding reasons for not providing a saliva sample. Indeed, the majority of cohort members (63.8%) who did not consent to provide a saliva sample skipped the survey question (Table 5).

Among those who did provide a response, the reason given was in most cases (53.8%) vague and uninformative; respondents expressed a general unwillingness or referred to “personal reasons”. For example, the open-ended responses in this group are

mostly classified as: “no reason”, “I don’t want to”, “I am not happy to”, “I prefer not to” or “I don’t agree to”.

Over one in four (26.9%) participants who provided a reason for opting not to consent described the concerns about the request being too intrusive or invasive or referred to privacy concerns. For example, they mentioned being uncomfortable with the request, stressed the sensitivity of the data collected and pointed out that researchers already hold excessive information on them.

Another relatively common reason for non-consent was lack of trust or a need for further reassurance. Approximately 10% of respondents who declined participation, and provided a reason for that, cited these concerns. Among these, some expressed uncertainty or discomfort with DNA storage and sharing for research purposes, a general mistrust in the data collection process, or a desire for additional assurances regarding data usage, handling of biological samples, and discomfort or concerns over the linkage of survey data with DNA information. Ethical considerations also contributed to their reluctance.

Finally, about 5% of respondents expressed concerns regarding the perceived lack of personal or public benefit from the saliva collection process. Some cohort members felt that the task was irrelevant and unnecessary. Additionally, a few participants highlighted the lack of adequate *personal* incentives, noting that the offered monetary incentive was insufficient (21 respondents) or expressed a desire for personalized feedback in return for their participation (18 respondents).

Table 5: Reasons for non-consenting, including and excluding non-respondents to this item

Reasons for non-consenting	% all	% valid
No interest or circumstantial reasons:	*1.8*	*4.7*
I don't have time or this task is too burdensome	0.9	2.3
I am not interested	0.6	1.7
I moved or I am abroad	0.3	0.7
Intrusiveness or invasiveness, and privacy concerns:	*9.9*	*26.9*
I feel uncomfortable, unsure, weird about providing saliva or DNA sample	4.8	13.0
The request is intrusive or invasive	1.9	5.0
Protection of privacy and privacy concerns	1.0	2.7
Researchers already have too much of my data	0.9	2.4
This data is too personal	0.8	2.2
I am worried about data breaches or what DNA might be used for in the future	0.3	0.9
Protection of personal data	0.2	0.6
This request is unexpected	0.0	0.1
Lack of personal or public benefit:	*1.7*	*4.7*
I don't see the relevance or the meaningful contribution or it feels unnecessary	1.2	3.2
The incentive amount is too low	0.3	0.8
I wish I would receive feedback or I want to know the results of DNA testing	0.2	0.7
Lack of trust / need for further reassurance:	*3.8*	*10.0*
I don't want or I am unsure about DNA being stored or shared for research	1.4	3.8
mistrust	1.1	2.9
I need more information or don't know how this data/sample will be used;	0.9	2.4
I am not comfortable or feeling unsafe about my DNA being stored overseas	0.2	0.5
I don't want my DNA and personal information collected together	0.1	0.2
ethical concerns	0.1	0.2
Vague answer:	*20*	*53.8*
no reason	10.6	28.5
I don't want to; I am not happy to; I prefer not to; I don't agree to	7.0	18.7
prefer not to say/no answer	0.7	2.0
Other	1.1	3.0
personal choice	0.5	1.2
I don't know	0.1	0.4
Missing	*63.8*	*N/A*
N	*7,279*	*2,716*

Conclusions

This paper describes the processes of collecting saliva samples for genotyping in a large-scale cohort study of young adults in England: the Next Steps Age 32 survey. First, we investigate the consent rates, return rates, and the quality of the samples for genotyping. Second, we analyse factors associated with consent and return rates and the role of monetary incentives. Finally, we identify reasons for non-consent, with the ultimate goal of identify recommendations for improving the saliva collection protocols and respondent materials for future studies.

Given that this was the first time this cohort had been requested to provide any kind of sample of objective health measurement the consent rate was regarded by the study team as satisfactory though somewhat lower than anticipated, with just under six in ten study participants agreeing to provide a saliva sample. However, only half of those who consented ultimately returned their sample to the laboratory. This low return rate, combined with a portion of saliva samples being unusable or of insufficient quality for genotyping, meant that DNA data are ultimately available for only one in four participants. This finding highlights the importance of factoring in potential losses in sample sizes when planning collection of saliva samples for genotyping. Overall, however, the end result was a sample of sufficient size for meaningful statistical analysis.

Comparing the consent and return rates from Next Steps with evidence from other studies is not straightforward. Gatny, Couper and Axinn (2013) report that participation rates in biosample collection across a number of studies vary widely (between 15% and 92%) but the evidence is hardly comparable as studies differ in type of biosample requested and biomarker investigated, mode in which the request is administered, survey year (with some dating back to the late 1990s), study characteristics (e.g. clinical *versus* survey) and, most notably, target population – some of which were very specific and likely associated with a higher participation propensity than the general population.

Most recently, evidence from another UK-based cohort study, the Millennium Cohort Study (MCS), showed genotyping rates of 78% among 14-years-olds (Fitzsimons et al. 2022). We consider a number of reasons which might explain the higher rates

observed in MCS. Firstly, the MCS study had a significant focus on health since its inception and the collection of biological samples and objective health measurements had been features of previous surveys. In addition, while MCS has always been an academically-led study, Next Steps was originally established by a government body, the Department for Education. A perception of the ongoing involvement of the Government may have exacerbated privacy concerns. In addition, MCS involved data collection, including saliva sample collection from parents as well as teenagers, so parents may have played a role in encouraging participation in this element of the study. Finally, all MCS data collection was conducted in-person, with interviewers collecting samples during home visits and returning samples to the lab directly. In Next Steps, only about 10.6% of our sample was surveyed in person by interviewer who would encourage participation and/or return the sample (87% completed by web or secondary device, and only about 2.2% *via* telephone or video interviewing). While respondent's self-selection into mode does not allow us to disentangle the role of mode of data collection, we notice a 7% higher return rates when the interviewer was in charge of returning the sample to the lab (i.e. in face-to-face versus web, secondary device, telephone, and video-interviewing); conversely, no significant differences by data collection mode were observed in consent rates. As web respondents are those that respond more promptly to the survey request (generally within the first three weeks) and hence are expected to be more cooperative and engaged in the study, it would be interesting to explore what their consent rates would have been had they been invited to provide the sample by an interviewer. Further research may attempt at disentangling mode effects and selection into mode, and to identify collection protocols to maximise informed consent and return rates in self-administration. A number of socio-demographic factors are associated with consent and return rates. White ethnicity is associated with higher odds of consenting to saliva collection; this result is consistent with findings from another UK cohort study of young people, i.e. the Age 14 Millennium Cohort Study (Fitzsimons et al. 2022), but in contrast with results on older age groups in the US (Sakshaug, Couper and Ofstedal 2010).

Educational level was not associated with adherence with the task. This is consistent with findings from Sakshaug, Couper and Ofstedal (2010), but are in contrast to the evidence from other studies (i.e. Dykema et al. 2016; Fitzsimons et al. 2022) which

find that the likelihood of providing a saliva sample is lower for individual with lower education.

Study participants living with a cohabiting partner showed higher odds of returning the sample (while no effect is found on consent). One possible interpretation of this finding is that the cohabiting partner may remind the study member to post the sample, though we cannot test this speculation. While in our study only the cohort member was asked to provide the sample, the finding is consistent with prior research finding higher cooperation among respondents living with one or more sample member eligible for the collection of physical measures, including saliva samples for genotyping (Sakshaug, Couper and Ofstedal 2010).

Cohort members in poorer health were more likely to consent to provide a saliva sample. This finding can be understood through the lens of leverage-saliency theory (Groves, Singer and Corning 2000), which suggests that among respondents facing health challenges the appeal of contributing to medical research may exert a stronger leverage in motivating consent. This interpretation aligns well with the emphasis in the informational leaflet on the relevance of DNA genotyping for advancing medical research. For instance, the leaflet highlighted the potential for these data to aid in "Helping treat common diseases" and referenced the contribution by the National Child Development Study to groundbreaking scientific discoveries and evidence for new treatments for common conditions like diabetes, bipolar disorder, and inflammatory diseases. However, once the respondent has consented, those who rated their health as "excellent" (versus "poor") are more likely to return the sample, and the net effect of health on returning the sample (on all eligible sample members) is not significant. With respect to the literature, findings on the association between health and consent to saliva collection for DNA extraction are mixed, with some studies suggesting lower participation by respondents with poorer health (Dykema et al. 2016) and other suggesting no association (Sakshaug, Couper and Ofstedal 2010).

Somewhat surprisingly, generalised trust in other people is not associated with consent to sample provision; however, as expected, it predicts higher return rates, signalling a higher adherence to the protocol. With respect to personality traits, the odds of agreeing to provide a saliva collection are higher for respondents scoring high on an agreeableness subscale, in line with our expectations. Other results on the

association between personality traits and compliance to the saliva collection task are mixed and to some extent unexpected. Contrary to our hypothesis, openness to new experiences and conscientiousness are not associated with consenting to provide a sample nor returning the sample to the lab; also, it remains unclear which underlying mechanisms could explain the slightly higher odds of sample return rates among respondents scoring higher on the neuroticism subscale. Finally, while we expected extroverted respondents to have higher odds of consenting and returning the sample, in light of the evidence that social integration is associated with higher participation in the saliva collection tasks (Dykema et al. 2016), the opposite seem to be true: respondents who scored higher in the extraversion subscale show slightly lower odds of returning the sample; effects are however small and the (currently) limited research in the area does not offer a clear framework for interpreting this evidence.

Not surprisingly, respondents' prior engagement in the study predicts compliance with the saliva collection protocol. Consistently with our hypothesis, and with the literature (Dykema et al. 2016), cohort members who participated in the prior survey wave had higher odds of returning the saliva sample to the laboratory. These findings underscore the value of the participant engagement initiatives undertaken within this cohort. One of the predictors of agreeing to providing a saliva sample is study participants' consent to linkage between survey data and health administrative records. In interpreting this result it is worth noting that study participants were asked several different data linkage requests (i.e. linkage to school records; information on higher education applications and offers; data on student loans; records on employment, earnings, tax credits, occupational pensions, and National Insurance Contributions; records of benefit claims and participation in employment programs; and criminal records). Data linkage consent rates are highly correlated with each other: that is the vast majority of cohort members consenting to linkage of survey data with health records also consented to linkage with other administrative data. Therefore, we interpret the higher compliance rates among participants who consented to data linkage as reflecting a greater overall commitment to the survey rather than a specific interest in health-related topics.

Reverse causality cannot be ruled out in interpreting the strong positive association between reading the saliva consent booklet and compliance: participants already inclined to consent may be more likely to consult the leaflet to understand the process,

while those firmly opposed may disregard the additional information provided. However, even among consenters to saliva collection, consulting the booklet was associated with higher odds of returning the sample, suggesting that the leaflet might have a role in reinforcing cohort members decision to send the sample to the laboratory. We recommend investing efforts in the careful drafting of such materials, to promote informed consent and support participant compliance.

With reference to the survey task, interviewer-administered mode of data collection was associated with a lower level of consent to provide a saliva sample: we interpret this finding in light of sample selection – i.e. less cooperative study participants tend to participate in later stages of fieldwork (i.e. during face-to-face data collection) and might be also less inclined to undertake in additional survey tasks such as saliva sample collection. Interviewers however play an important role in ensuring that samples are shipped back to the laboratory, as such we encourage extensive interviewer training.

In line with a vast body of research on the role of monetary incentives in promoting survey participation (for a recent review see: Gaia et al. 2024b) we find that higher monetary incentives lead to significantly higher levels of consent to provide a saliva sample and increased likelihood of returning the sample to the lab. The effects are substantial, with an increase of around 5 percentage points in consent rates and nearly 13 percentage points in sample return rates. This significant impact clearly supports the decision to raise the incentive from £5 to £10.

The reasons given by participants who opted not to provide a saliva sample are not particularly informative. In most cases either no reason is reported, or a vague answer is given. This evidence suggests that decisions may often be circumstantial rather than being a reflective decision, where participants evaluate the risks and benefits of their choice. In this respect, the decision making process behind consent to providing a saliva sample seem to resemble to some extent that process behind data linkage consent requests – as outlined by the (empirically tested) motivational framework proposed by Burton et al. (2021), which shows that study participants are often guided by circumstantial reasons or gut feelings in deciding whether to allow linkage between survey data and administrative records. This interpretation is also supported by the aforementioned strong impact of the monetary incentive increase: if an additional £5

incentive has such a strong effect on consent and return rates, the cohort members motivations may not be so deeply rooted.

Despite the many lessons learned, this research has a number of limitations. First, these finding are limited to a relatively homogeneous cohort of young people aged 32 years old; further research may investigate willingness to provide saliva samples for DNA extraction and evaluate collection protocols amongst other age groups.

Secondly, although the change in the value of the incentive offered between the first batch (soft-launch) of fieldwork and batches 1-3, allows us to explore the impact of an incentive increase, the change in incentive was implemented alongside other minor saliva collection protocol changes and we are not able to disentangle the impact of each.

Third, the overall study monetary incentive protocol shifted from a targeted incentive design (in the soft launch) to a standard design (in batches 1-3). Although research found no significant differences in survey response and bias across the two monetary incentives designs in this survey wave (Gaia et al. 2024b), the marginal impact of the saliva incentive may vary depending on monetary incentive offered for survey participation.

Finally, participants took part in the study in a range of modes. As participants self-selected into mode we are not able to disentangle selection effects and fully assess how mode of interview could affect consent and return rates of samples.

While our study addresses important research gaps, a number of research questions remain unanswered. An area of research that remains underexplored is the potential impact of saliva collection requests for genotyping on survey participation and attrition. Preliminary findings from a cohort study of infants in their first year of life (the Early Life Cohort Study), found that response rates were similar between an experimental group asked to provide saliva for DNA genotyping and a control group (Calderwood et al. 2024). This is in contrast with some very early work (Etter, Perneger and Ronchi 1998) on a very specific population (students, faculty, and staff members of Geneva University) finding lower response rates to a mail questionnaire when a saliva consent request was included (not for genotyping). With respect to attrition, the evidence is scarce and mixed. Gatny, Couper and Axinn (2013) found no effect on attrition of being requested and providing a saliva sample, even though this evidence is based on a

specific population (young women who reported the end of a romantic relationship). Conversely, Pashazadeh, Cernat and Sakshaug (2021) found higher attrition in the subsequent wave among participants to a nurse visit in a large-scale UK based household study (Understanding Society: the UK Household Longitudinal Study) but no long-term effect was found. Finally, Lawes et al. (2024) found that *providing* a biological sample was positively associated with long-term study participation, but they could not assess whether the *request* itself has an effect on attrition.

Furthermore, currently, a widely recognized ethical framework for the collection of biomarkers does not exists (Weir 2018). Discussion is needed on best practices for respondents' confidentiality, the appropriateness of offering conditional monetary incentives in invitations to provide biological samples for genotyping, as well as on the way to collect consent (by signed forms, orally, at the click of a button) for different types of populations under study, biomarker collected and timeframe for which consent is sought – on the latter see: Chen et al. (2005). Such practices should also comply with legislation, which may change across countries or regions, complicating cross-national research (see aslo: Haga and Beskow 2008).

Finally, as recently advocated by Kumari and Benzeval (2021), further research may adopt the Total Survey Error (TSE) framework for the analysis of trade-offs in different sources of survey error in the collection of biological samples.

By documenting the efforts of large-scale probability-based cohort studies in implementing biological sample collection, empirically assessing consent and return bias and testing the effectiveness of incentives in increasing consent and return rates, this study contributes to the improving protocols for collecting saliva sample for genotyping.

References

Burton, Jonathan, Mick P. Couper, Thomas F. Crossley, Annette Jäckle and Sandra Walzenbach. 2021. “How Do Survey Respondents Decide Whether to Consent to Data Linkage?” Institute for Social and Economic Research, Understanding Society Working Paper, 2021-05.

Calderwood, Lisa, Nickie Rose, Susan Ring and Wendy McArdle. 2014. “Collecting Saliva Samples for DNA Extraction from Children and Parents: Findings from a Pilot Study Using Lay Interviewers in the UK.” *Survey Methods: Insights from the Field*. doi: 10.13094/SMIF-2014-00002.

Calderwood, Lisa, Alissa Goodman, Pasco Fearon, Erica Wong, Alyce Raybould, Karen Dennison, Richard Silverwood, Charlotte Booth and Konstantinos Tsigaridis. 2024. “Innovation, Engagement and Inclusivity: A Feasibility Study for a New UK Birth Cohort.” Paper presented at the ESS-Natcen Methods Seminars, 20 November 2024, London.

Centre for Longitudinal Studies. 2024. “CLS Genomics Data”. Retrieved 13 December 2024, (https://cls-genetics.github.io/docs/intro.html).

Chen, Donna T, Donald L Rosenstein, Palaniappan Muthappan, Susan G Hilsenbeck, Franklin G Miller, Ezekiel J Emanuel and David Wendler. 2005. “Research with Stored Biological Samples: What Do Research Participants Want?”. *Archives of Internal Medicine* 165(6):652-55.

Dykema, Jennifer, Kerryann DiLoreto, Kenneth D. Croes, Dana Garbarski and Jeremy Beach. 2016. “Factors Associated with Participation in the Collection of Saliva Samples by Mail in a Survey of Older Adults.” *Public Opinion Quarterly* 81(1):57-85.

Etter, Jean-François, Thomas V. Perneger and Anne Ronchi. 1998. “Collecting Saliva Samples by Mail.” *American Journal of Epidemiology* 147(2):141-46.

Fitzsimons, Emla, Vanessa Moulton, David A Hughes, Sam Neaves, Karen Ho, Gibran Hemani, Nicholas Timpson, Lisa Calderwood, Emily Gilbert and Susan Ring. 2022. “Collection of Genetic Data at Scale for a Nationally Representative Population: The Uk Millennium Cohort Study.” *Longitudinal and Life Course Studies* 13(1):169-87.

Gaia, Alessandra, Matt Brown, Adali Tugba, Stella Fleetwood and Christy Lai. 2024a. “Response burden and survey participation: experimental evidence on the effect of

interview length on non-response conversion." Centre for Longitudinal Studies, CLS Working Paper Series, 2024/5.

Gaia, Alessandra, Matt Brown, Adali Tugba, Stella Fleetwood and Christy Lai. 2024b. "The Effect of Targeted Incentives on Response Rates and Representativeness: Evidence from the Next Steps Age 32 Survey." Centre for Longitudinal Studies, CLS Working Paper Series, 2024/4.

Gatny, Heather H, Mick P. Couper and William G Axinn. 2013. "New Strategies for Biosample Collection in Population-Based Social Research." *Social Science Research* 42(5):1402-09.

Groves, Robert M. and Mick P. Couper. 2012. *Nonresponse in Household Interview Surveys*: Hoboken, NJ: John Wiley & Sons.

Groves, Robert M., Eleanor Singer and Amy Corning. 2000. "Leverage-Saliency Theory of Survey Participation: Description and an Illustration." *Public Opinion Quarterly* 64(3):299-308.

Haga, Susanne B and Laura M Beskow. 2008. "Ethical, Legal, and Social Implications of Biobanks for Genetics Research." *Advances in Genetics* 60:505-44.

Ipsos. 2024. "Next Steps - Sweep 9 Survey Technical Report." Ipsos. Retrieved January 17, 2025 (https://doc.ukdataservice.ac.uk/doc/5545/mrdoc/pdf/next_steps_sweep_9_age_32_technical_report.pdf)

Kumari, Meena and Michaela Benzeval. 2021. "Collecting Biomarker Data in Longitudinal Surveys." Pp. 26-46 in *Advances in Longitudinal Survey Methodology*, edited by P. Lynn. Hoboken, NJ: Wiley.

Lawes, Mario, Clemens Hetschko, Joseph W. Sakshaug and Michael Eid. 2024. "Collecting Hair Samples in Online Panel Surveys: Participation Rates, Selective Participation, and Effects on Attrition." *Survey Research Methods*, 18(2): 167–185. doi: 10.18148/srm/2024.v18i2.8170.

Pashazadeh, Fiona, Alexandru Cernat and Joseph W. Sakshaug. 2021. "The Effects of Biological Data Collection in Longitudinal Surveys on Subsequent Wave Cooperation." Pp. 100-21 in *Advances in Longitudinal Survey Methodology*, edited by P. Lynn. Hoboken, NJ: Wiley.

Sakshaug, Joseph W., Mick P. Couper and Mary Beth Ofstedal. 2010. “Characteristics of Physical Measurement Consent in a Population-Based Survey of Older Adults.” *Medical Care* 48(1):64-71.

Shireby, Gemma, Tim T Morris, Andrew Wong, Nish Chaturvedi, George B Ploubidis, Emla Fitzsimmons, Alissa Goodman, Adelaida Sanchez-Galvez, Neil M Davies, Liam Wright and David Bann. 2024. “Data Resource Profile: Genomic Data in Multiple British Birth Cohorts (1946-2001)—Health, Social, and Environmental Data from Birth to Old Age.” *medRxiv*. doi:10.1101/2024.11.06.24316761

University College London, UCL Institute of Education and Centre for Longitudinal Studies. 2024. “Next Steps: Sweeps 1-9, 2004-2023. [Data Collection].” *17th Edition*. UK Data Service, 2024 [Accessed 30 August 2024]. doi: 10.5255/UKDA-SN-5545-9.

Weir, David. 2018. “Biomarkers in Representative Population Surveys.” Pp. 227-33 in *The Palgrave Handbook of Survey Research* edited by D. Vannette and J. Krosnick. Cham, Switzerland: Palgrave Macmillan. doi: 10.1007/978-3-319-54395-6_29.

Wu, Alison Fang-Wei, Morag Henderson, Matt Brown, Tugba Adali, Richard J Silverwood, Darina Peycheva and Lisa Calderwood. 2024. “Cohort Profile: Next Steps—the Longitudinal Study of People in England Born in 1989–90.” *International Journal of Epidemiology* 53(6). doi: 10.1093/ije/dyae152.