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Data Resource Profile: The Statistics of the Korea National Health and Nutrition Examination Survey (KNHANES) Biobank Project

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ABSTRACT

The Korea National Health and Nutrition Examination Survey (KNHANES) is a representative survey of the Korean population, providing evidence for health policy and health interest statistics. The survey is conducted annually, and the 10th cycle, 1st year (2025) survey is currently underway. In health examination of KNHANES, blood samples are collected from people aged 10 years or older, and urine samples are collected from people aged 6 years or older. To support research related to various public health concerns based on the general population, the National Bank of Korea (NBK) has been operating the KNHANES biobank project since 2005 and has distributed high-quality biospecimens collected through KNHANES. To date, biospecimens from a total of 95,455 participants have been deposited, with approximately 35,500 biospecimens available as of December 2024. This biobank provides serum, plasma, and extracted DNA to researchers in officially approved projects. Recently, urine specimens have also become available. Additionally, genotyping data (> 833,000 genetic markers) for ~19,300 participants generated from the KoreanChip are available. The vast epidemiological data linkage derived from KNHANES will provide valuable insights into public health issues. Researchers can access the resource through NBK's online platform (HuBIS_Desk, https://biobank.nih.go.kr/Desk/).

Keywords: Biobank; Biospecimen; Korea National Health and Nutrition Examination Survey; National Biobank of Korea; Population-Based Biobanking



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Disclosure

The authors have no potential conflicts of interest to disclose.

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INTRODUCTION

The Korea National Health and Nutrition Examination Survey (KNHANES) began in 1998 and is a representative survey of Koreans that investigates health status, health behaviors, and nutritional intake for statistical purposes. It consists of health interview, health examination, and nutritional survey focused on age-specific public health concerns. The survey cycle is planned for three-year units and the survey is conducted annually to produce timely statistics.¹ The 10th cycle, 1st year survey (2025) is currently underway. Data collected through the KNHANES are used as evidence for health policy and are publicly available to researchers. More information about KNHANES can be found elsewhere.²-3

To improve human health, several countries have established and are operating population-based biobanking systems, such as the US National Health and Nutrition Examination Survey Biospecimen Program, Statistics Canada Biobank, and Australian Health Biobank, that collect biospecimens from national surveys. In Korea, the National Bank of Korea (NBK) collects and distributes high-quality, diverse human biospecimens from population-based and disease-based participants. The NBK has been operating the KNHANES biobank project since 2005 to utilize blood and urine specimens collected through the KNHANES for health research, with the consent of the participants. The primary purpose of this biobank is to support research related to various public health interests, such as chronic disease and emerging infectious disease research, environmental exposure assessment, and nutritional status monitoring, by utilizing collected human bioresources. It provides extracted DNA and genotyped data based on the KoreanChip, and is conducting a demand survey to enhance resource utilization. Currently, bioresources collected in the 6th (2013–2015), 7th (2016–2018), 8th (2019–2021), and 9th (2022) survey cycles are available to researchers who request them. It is expected to continue to expand in the future as the KNHANES is conducted.

In this article, based on completed survey cycle data, we aim to provide basic resource profile to increase understanding of the KNHANES biobank project and to activate its health-related research use.

DATA RESOURCE BASICS

Collection and storage of biospecimen

The sample of KNHANES, which is conducted annually, is newly selected for each cycle, targeting people aged 1 year or older. The number of participants and response rate by survey cycle were 22,948 (78.3%) for the 6th, 24,269 (76.6%) for the 7th, and 22,559 (74.0%) for the 8th, respectively. In health examination, blood samples are collected from people aged 10 years or older, and urine samples are collected from people aged 6 years or older. Distribution of urine resources began with biospecimens collected during the 9th survey cycle. Of them, the KNHANES biobank project stores biospecimens from individuals who have provided consent for long-term storage and use for future research in the public interest. Accordingly, as of December 2024, the number of participants with available biospecimens for each survey cycle in this national biobank is 8,515 for the 6th, 9,527 for the 7th, and 11,745 for the 8th. An overview of the number and types of available biospecimens is listed in Table 1. For long-term storage, serum and plasma were aliquoted into 6 to 7 vials of 0.3 mL each. Genomic DNA was extracted using the G-DEX™ IIb Genomic DNA Extraction Kit (iNtRON Biotechnology, Seongnam, Korea). Four DNA aliquots were generated per



Table 1. Overview of available biospecimens from each the KNHANES cycle

| Types | Sex | Age range, | Survey cycle | | | | | | | | | | |
|---|--------|------------|--------------|------|------|-------------|------|-------|-------|--------------|-------|--|--|
| | | yr | KNHANES VI | | | KNHANES VII | | | | KNHANES VIII | | | |
| | | | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | | |
| Serum | Male | 10-18 | 34 | 47 | 53 | 27 | 72 | 88 | 133 | 143 | 82 | | |
| | | 19-39 | 146 | 421 | 379 | 417 | 425 | 596 | 651 | 636 | 439 | | |
| | | 40+ | 572 | 872 | 933 | 804 | 951 | 1,295 | 1,346 | 1,335 | 1,030 | | |
| | Female | 10-18 | 67 | 18 | 28 | 13 | 53 | 84 | 96 | 88 | 63 | | |
| | | 19-39 | 398 | 418 | 361 | 346 | 359 | 589 | 573 | 610 | 372 | | |
| | | 40+ | 935 | 952 | 886 | 788 | 959 | 1,461 | 1,555 | 1,472 | 1,035 | | |
| Plasma | Male | 10-18 | 62 | 49 | 60 | 28 | 71 | 89 | 134 | 141 | 82 | | |
| | | 19-39 | 423 | 422 | 411 | 426 | 434 | 592 | 646 | 637 | 442 | | |
| | | 40+ | 925 | 883 | 963 | 833 | 971 | 1,292 | 1,352 | 1,337 | 1,046 | | |
| | Female | 10-18 | 78 | 18 | 31 | 15 | 55 | 84 | 97 | 87 | 64 | | |
| | | 19-39 | 443 | 428 | 398 | 368 | 370 | 592 | 573 | 612 | 376 | | |
| | | 40+ | 1,020 | 965 | 932 | 818 | 982 | 1,463 | 1,563 | 1,475 | 1,047 | | |
| Extracted DNA | Male | 10-18 | 58 | 49 | 60 | 27 | 72 | 79 | 133 | 142 | 82 | | |
| | | 19-39 | 418 | 420 | 410 | 346 | 432 | 534 | 651 | 629 | 441 | | |
| | | 40+ | 912 | 878 | 961 | 708 | 965 | 1,152 | 1,345 | 1,321 | 1,045 | | |
| | Female | 10-18 | 76 | 18 | 31 | 15 | 54 | 79 | 97 | 87 | 64 | | |
| | | 19-39 | 436 | 425 | 397 | 310 | 367 | 538 | 569 | 599 | 374 | | |
| | | 40+ | 1,004 | 958 | 927 | 703 | 974 | 1,318 | 1,539 | 1,442 | 1,041 | | |
| Genotyped data (Korean chip ver 1.1) | Male | 10-18 | 54 | 47 | 52 | 27 | 69 | 72 | 72 | - | - | | |
| | | 19-39 | 404 | 413 | 392 | 341 | 426 | 505 | 426 | - | - | | |
| | | 40+ | 894 | 860 | 934 | 700 | 943 | 1,095 | 895 | - | - | | |
| | Female | 10-18 | 73 | 18 | 27 | 15 | 50 | 71 | 61 | - | - | | |
| | | 19-39 | 426 | 413 | 376 | 305 | 358 | 510 | 355 | - | - | | |
| | | 40+ | 972 | 933 | 899 | 693 | 957 | 1,261 | 914 | - | - | | |

Numbers in the table indicate the number of participants with biospecimens available for distribution as of December 2024. KNHANES = Korea National Health and Nutrition Examination Survey.

individual; $20 \mu g$ in 2 vial, $5 \mu g$ in 1 vial, and the remaining DNA in 1 vial. Urine was also aliquoted into 10 vials of 1 mL. Collected biospecimens are stored and managed at NBK under optimal temperatures for biospecimen type.

Quality management of biospecimens

NBK operates a backup bank to safely preserve human resources from unexpected disasters and accidents, and biospecimens are managed based on standard operation procedures.⁷ For quality control, on-site inspections (internal and external quality control), measurement traceability evaluation, inter-laboratory comparison, and stability and reproducibility evaluation of short-term and long-term storage are conducted. Quality control of biospecimens collected through the KNHANES is systematically performed, and detailed descriptions and results of the tests are reported annually through a quality control report. To ensure high quality of biospecimens, NBK participated in the international proficiency-testing program hosted by the International Society of Biological and Environmental Repositories in 2019 and received a 'very satisfactory' rating.

Data resource coverage

The vast data collected at the individual level through KNHANES is available to researchers as data resources. All data is provided anonymized to protect the privacy of participants. Including anthropometric measures, biochemical profile data, data on socioeconomic position, lifestyle, medical condition, nutritional intake, etc. collected through structured questionnaires are also available. An overview of the epidemiological data and clinical laboratory measures collected by KNHANES is provided in **Supplementary Tables 1** and **2**. Detailed information can be found in the analytic guidelines/codebook posted on the KNHANES



Table 2. Scale of epidemiological data that can be linked to available biospecimens among the KNHANES biobank project participants

| Epidemiological data | Type of | Survey cycle | | | | | | | | | | |
|----------------------|---|--------------|------------|-------|-------|------------|-------|--------------|-------|-------|--|--|
| | biospecimens | | KNHANES VI | | | KNHANES VI | I | KNHANES VIII | | | | |
| | | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | | |
| Health interview & | Overall | 2,951 | 2,766 | 2,798 | 2,493 | 2,890 | 4,144 | 4,387 | 4,295 | 3,063 | | |
| Health examination | Serum | 2,152 | 2,728 | 2,640 | 2,395 | 2,819 | 4,113 | 4,354 | 4,284 | 3,021 | | |
| | Plasma | 2,951 | 2,765 | 2,795 | 2,488 | 2,883 | 4,112 | 4,365 | 4,289 | 3,057 | | |
| | Extracted DNA | 2,904 | 2,748 | 2,786 | 2,109 | 2,864 | 3,700 | 4,334 | 4,220 | 3,047 | | |
| | Genotyped data (Korean chip ver 1.1) | 2,823 | 2,684 | 2,680 | 2,081 | 2,803 | 3,514 | 2,723 | - | - | | |
| Health interview & | Overall | 2,648 | 2,475 | 2,516 | 2,114 | 2,508 | 3,635 | 3,821 | 3,373 | 2,515 | | |
| Health examination & | Serum | 1,973 | 2,441 | 2,371 | 2,030 | 2,447 | 3,610 | 3,793 | 3,362 | 2,480 | | |
| Nutrition survey | Plasma | 2,648 | 2,474 | 2,513 | 2,111 | 2,502 | 3,607 | 3,802 | 3,370 | 2,510 | | |
| | Extracted DNA | 2,606 | 2,457 | 2,506 | 1,794 | 2,485 | 3,245 | 3,775 | 3,325 | 2,502 | | |
| | Genotyped data (Korean chip ver 1.1) | 2,531 | 2,401 | 2,410 | 1,773 | 2,439 | 3,081 | 2,366 | - | - | | |

Numbers in the table indicate the number of participants with biospecimens available for distribution as of December 2024. KNHANES = Korea National Health and Nutrition Examination Survey.

website (https://knhanes.kdca.go.kr/knhanes/) or in the Resources section of the NBK website (https://biobank.nih.go.kr/cmm/main/mainPage.do). Genotyped data derived from KoreanChip consisting of over 833,000 single nucleotide polymorphisms (SNPs) are available from this biobank. Additionally, to increase the usability for research purposes, 26 biochemical markers were measured and provided from biospecimens of 8,248 participants in the 6th survey cycle. The list of 26 biomarkers and their measurement information can be found in **Supplementary Table 3**.

DATA RESOURCE PROFILE AND ACHIEVEMENT

Biospecimens collection of the KNHANES biobank project

As of December 2024, available biospecimens are listed by age and survey cycle in **Table 1**. The number of participants with biospecimens available for distribution in this biobank for each survey period was 8,515, 9,527, and 11,745, respectively. This corresponds to the proportion of KNHANES biobank project among KNHANES participants of 41.6%, 44.1%, and 57.0%, respectively. The male to female ratios were even at 0.97, 1.00, and 0.99, respectively. The availability of biospecimens varies depending on the type of biospecimen. The sizes of human biospecimens that could be matched to epidemiological data collected through KNHANES are presented in **Table 2**.

We summarized the demographic characteristics of the KNHANES participants and those of the KNHANES biobank participants. Since the number of biobank project participants with available biospecimens varied, we defined KNHANES biobank project participants as those with available genotyped data matched to epidemiological data collected through health interviews and health examinations. Based on the definition, we calculated the statistics accordingly. At present, the KNHANES biobank does not provide recalibrated survey weights to ensure the national representativeness of the biobank sample. Therefore, the statistics for KNHANES participants were expressed as weighted percentages with 95% confidence intervals, reflecting the complex sampling design of the survey, while those for the KNHANES biobank participants were presented as unweighted counts and percentages.



Participant characteristics of the KNHANES biobank project

Demographic characteristics of the KNHANES participants and the KNHANES biobank participants are presented in **Table 3**. Most biobank participants resided in Seoul, followed by Busan, with a high proportion living in urban areas. The age distribution showed the highest proportion in the 50–59 age group and the lowest in the 10–18 age group.

Clinical biomarker data derived from the KNHANES biobank project

This biobank provides data by measuring biochemical markers related to various categories of chronic diseases. **Table 4** presents statistics on 26 biochemical markers measured in biospecimens from 8,248 participants in the sixth survey cycle. Of these, 4,025 were male

Table 3. Participant characteristics of epidemiological data & genotypic integrated data among KNHANES biobank project participants

| Variables | KNHANES VI | | | | | KNHANES VII | | | | | KNHANES VIII | | | | |
|-------------------|--------------------------------|------|-----------------|---|------|--------------------------------|------|---|-------|--------------------------------|---------------|---|-----------------|-------|------|
| | Statistics from the KNHANES | | | Statistics from the KNHANES biobank projects | | Statistics from the KNHANES | | Statistics from the KNHANES biobank projects | | Statistics from the KNHANES | | Statistics from the KNHANES biobank projects | | | |
| | Weighted % | | Upper 95% CI | No. | % | Weighted % | | Upper 95% CI | No. | % | Weighted % | Lower 95% CI | Upper 95% CI | No. | % |
| Sex | | | | | | | | | | | | | | | |
| Male | 49.9 | 49.2 | 50.6 | 4,050 | 49.5 | 50.0 | 49.3 | 50.7 | 4,178 | 49.8 | 50.0 | 49.4 | 50.6 | 1,393 | 51.2 |
| Female | 50.1 | 49.4 | 50.8 | 4,137 | 50.5 | 50.0 | 49.3 | 50.7 | 4,220 | 50.3 | 50.0 | 49.4 | 50.6 | 1,330 | 48.8 |
| Age, yr | | | | | | | | | | | | | | | |
| 10-18 | 11.2 | 10.7 | 11.8 | 271 | 3.3 | 10.0 | 9.4 | 10.6 | 304 | 3.6 | 8.8 | 8.3 | 9.4 | 133 | 4.9 |
| 19-29 | 16.4 | 15.5 | 17.3 | 991 | 12.1 | 15.9 | 15.0 | 16.8 | 1,089 | 13.0 | 15.7 | 14.9 | 16.6 | 341 | 12.5 |
| 30-39 | 17.0 | 16.0 | 17.9 | 1,433 | 17.5 | 16.1 | 15.1 | 17.1 | 1,356 | 16.2 | 15.1 | 14.1 | 16.1 | 440 | 16.2 |
| 40-49 | 18.5 | 17.8 | 19.3 | 1,576 | 19.3 | 18.3 | 17.6 | 19.0 | 1,715 | 20.4 | 17.4 | 16.6 | 18.1 | 501 | 18.4 |
| 50-59 | 17.3 | 16.5 | 18.0 | 1,793 | 21.9 | 17.9 | 17.1 | 18.6 | 1,823 | 21.7 | 18.0 | 17.2 | 18.7 | 549 | 20.2 |
| 60-69 | 10.0 | 9.5 | 10.6 | 1,412 | 17.3 | 11.6 | 11.0 | 12.3 | 1,468 | 17.5 | 13.6 | 12.9 | 14.3 | 518 | 19.0 |
| 70+ | 9.5 | 8.9 | 10.1 | 711 | 8.7 | 10.2 | 9.5 | 10.8 | 643 | 7.7 | 11.4 | 10.6 | 12.2 | 241 | 8.9 |
| Region | | | | | | | | | | | | | | | |
| Seoul | 19.9 | 19.1 | 20.7 | 1,428 | 17.4 | 19.3 | 18.4 | 20.1 | 1,549 | 18.4 | 18.8 | 17.8 | 19.8 | 505 | 18.6 |
| Busan | 6.9 | 6.3 | 7.5 | 525 | 6.4 | 6.7 | 6.1 | 7.4 | 782 | 9.3 | 6.5 | 5.9 | 7.1 | 199 | 7.3 |
| Daegu | 4.9 | 4.5 | 5.4 | 499 | 6.1 | 4.8 | 4.1 | 5.5 | 401 | 4.8 | 4.7 | 4.0 | 5.4 | 142 | 5.2 |
| Incheon | 5.6 | 4.9 | 6.3 | 418 | 5.1 | 5.7 | 5.0 | 6.4 | 441 | 5.3 | 5.7 | 4.9 | 6.5 | 154 | 5.7 |
| Gwangju | 3.0 | 2.2 | 3.8 | 282 | 3.4 | 4.0 | 3.0 | 4.9 | 256 | 3.1 | 3.3 | 2.4 | 4.1 | 58 | 2.1 |
| Daejeon | 3.5 | 2.5 | 4.4 | 309 | 3.8 | 3.8 | 2.5 | 5.0 | 246 | 2.9 | 3.4 | 2.1 | 4.7 | 74 | 2.7 |
| Ulsan | 2.3 | 1.1 | 3.6 | 208 | 2.5 | 2.4 | 1.1 | 3.6 | 226 | 2.7 | 2.2 | 1.0 | 3.5 | 47 | 1.7 |
| Sejong | - | - | - | - | - | 0.5 | 0.4 | 0.5 | 143 | 1.7 | 0.7 | 0.6 | 0.8 | 54 | 2.0 |
| Gyeonggi | 24.0 | 23.1 | 24.9 | 1,979 | 23.0 | 24.7 | 23.6 | 25.8 | 1,894 | 22.6 | 25.6 | 24.4 | 26.9 | 660 | 24.2 |
| Gangwon | 3.1 | 2.2 | 4.0 | 296 | 3.6 | 2.8 | 1.8 | 3.8 | 255 | 3.0 | 3.1 | 1.7 | 4.5 | 109 | 4.0 |
| Chungbuk | 2.9 | 2.4 | 3.5 | 274 | 3.4 | 2.7 | 2.2 | 3.3 | 206 | 2.5 | 3.0 | 2.3 | 3.7 | 61 | 2.2 |
| Chungnam | 4.1 | 3.0 | 5.2 | 291 | 3.6 | 3.8 | 2.5 | 5.1 | 234 | 2.8 | 3.8 | 2.6 | 5.1 | 93 | 3.4 |
| Jeonbuk | 3.5 | 2.4 | 4.7 | 263 | 3.2 | 3.6 | 2.3 | 5.0 | 233 | 2.8 | 3.3 | 2.0 | 4.5 | 74 | 2.7 |
| Jeonnam | 3.4 | 2.1 | 4.7 | 247 | 3.0 | 2.6 | 1.6 | 3.7 | 246 | 2.9 | 3.3 | 2.0 | 4.6 | 110 | 4.0 |
| Gyeongbuk | 5.2 | 4.2 | 6.1 | 579 | 7.1 | 5.5 | 4.2 | 6.7 | 525 | 6.3 | 5.0 | 3.6 | 6.4 | 127 | 4.7 |
| Gyeongnam | 6.3 | 5.1 | 7.6 | 523 | 6.4 | 6.4 | 4.8 | 7.9 | 617 | 7.4 | 6.4 | 4.9 | 7.8 | 178 | 6.5 |
| Jeju | 1.3 | 0.9 | 1.6 | 166 | 2.0 | 0.9 | 0.6 | 1.3 | 144 | 1.7 | 1.2 | 0.8 | 1.6 | 78 | 2.9 |
| Area of residence | | | | | | | | | | | | | | | |
| Urban | 82.3 | 79.4 | 85.3 | 6,521 | 79.7 | 85.3 | 82.6 | 88.0 | 6,868 | 81.8 | 84.2 | 81.4 | 87.0 | 2,213 | 81.3 |
| Rural | 17.7 | 14.7 | 20.6 | 1,666 | 20.4 | 14.7 | 12.0 | 17.4 | 1,530 | 18.2 | 15.8 | 13.0 | 18.6 | 510 | 18.7 |
| Household income | 9 | | | | | | | | | | | | | | |
| Low | 15.5 | 14.4 | 16.5 | 1,211 | 14.9 | 15.5 | 14.4 | 16.6 | 1,093 | 13.0 | 14.3 | 13.3 | 15.3 | 404 | 14.9 |
| Middle low | 25.0 | 23.7 | 26.3 | 2,034 | 25.0 | 23.7 | 22.5 | 24.8 | 2,031 | 24.2 | 23.7 | 22.5 | 25.0 | 685 | 25.3 |
| Middle high | 29.7 | 28.3 | 31.0 | 2,343 | 28.8 | 29.6 | 28.4 | 30.8 | 2,507 | 29.9 | 29.2 | 28.0 | 30.4 | 735 | 27.1 |
| High | 29.8 | 28.1 | 31.6 | 2,558 | 31.4 | 31.2 | 29.5 | 33.0 | 2,749 | 32.8 | 32.7 | 30.9 | 34.6 | 889 | 32.8 |

This statistic was estimated for participants aged 10 years and older.

The definition of subjects for statistical analysis includes individuals who can be linked across health interview, health examination, and genotyped data. KNHANES = Korea National Health and Nutrition Examination Survey, CI = confidence interval.



Table 4. Summary statistics for 26 clinical biomarkers (overall)

| Variables | Total (N = 8,248) | Male (n = 4,025) | Female (n = 4,223) |
|---------------------------------------|------------------------------------|-----------------------------------|------------------------------------|
| Albumin, g/dL | 4.73 ± 0.29 [1.9-5.9] | $4.78 \pm 0.30 [1.9 - 5.9]$ | $4.68 \pm 0.27 [3.6 - 5.8]$ |
| Alkaline phosphatase, U/L | 71.77 ± 29.77 [15-495] | 75.59 ± 32.71 [15-495] | 68.14 ± 26.17 [15-388] |
| Apolipoprotein A, mg/dL | $148.24 \pm 26.26 [76-287]$ | 143.22 ± 25.81 [77-282] | $153.01 \pm 25.80 [76-287]$ |
| Apolipoprotein B, mg/dL | 102.31 ± 26.78 [21-305] | 103.89 ± 26.22 [21-198] | 100.80 ± 27.23 [28-305] |
| Calcium, mg/dL | $9.61 \pm 0.41 [6.0-11.6]$ | $9.66 \pm 0.41 [7.1-11.3]$ | $9.56 \pm 0.41 [6.0-11.6]$ |
| C-peptide, ng/mL ^a | 1.80 (1.40-2.40) [0.1-12.6] | 1.90 (1.50-2.50) [0.1-12.5] | 1.70 (1.40-2.20) [0.1-12.6] |
| CTx, ng/mL ^a | 0.42 (0.30-0.58) [0.05-6.00] | 0.44 (0.32-0.61) [0.09-2.73] | 0.39 (0.28-0.55) [0.05-6.0] |
| Cystatin-C, mg/L | $0.85 \pm 0.21 [0.38 - 9.68]$ | $0.90 \pm 0.24 [0.54 - 9.68]$ | $0.80 \pm 0.17 [0.38-5.69]$ |
| Direct bilirubin, mg/dL | 0.21 (0.16-0.28) [0.10-3.92] | 0.24 (0.18-0.31) [0.10-3.92] | 0.19 (0.15-0.25) [0.10-2.42] |
| Iron, μg/dL | 114.13 ± 46.92 [11-352] | 125.86 ± 49.38 [17-352] | 102.95 ± 41.47 [11-319] |
| Ferritin, ng/mL | 133.94 ± 134.32 [1.6-4,426.0] | 193.88 ± 156.04 [5.7-4,426.0] | 76.81 ± 73.13 [1.6-1,993.0] |
| Folate, ng/mL | 8.29 ± 4.79 [1.02-65.00] | $6.97 \pm 4.16 [1.02-57.60]$ | 9.54 ± 5.01 [1.49-65.00] |
| γ-GT, U/L | 21.00 (14.00-37.00) [6-2,773] | 31.00 (20.00-54.00) [6-2,773] | 16.00 (12.00-23.00) [6-905] |
| Homocysteine, μmol/L | 10.22 ± 5.21 [2.16-209.90] | $12.04 \pm 6.46 [4.41-209.90]$ | 8.49 ± 2.64 [2.16-46.60] |
| hs-CRP, mg/L | $1.33 \pm 4.00 [0.01 - 144.58]$ | $1.44 \pm 4.37 [0.01 - 144.58]$ | 1.23 ± 3.61 [0.10-118.45] |
| Insulin, µU/mL | 7.20 (4.90-10.70) [0.4-315.7] | 7.20 (4.90-10.90) [0.5-315.7] | 7.20 (5.00-10.60) [0.4-130.6] |
| Lipoprotein(a), mg/dL | $15.03 \pm 19.51 [0.4-191.6]$ | 13.04 ± 17.49 [0.4-160.0] | $16.93 \pm 21.09 [0.4-191.6]$ |
| Osteocalcin, ng/mL ^a | 18.13 ± 10.31 [1.48-230.70] | 18.36 ± 11.45 [3.67-230.70] | 17.90 ± 9.00 [1.48-160.70] |
| Phosphorus, mg/dL | $3.70 \pm 0.55 [2.0-7.2]$ | 3.58 ± 0.58 [2.0-7.2] | $3.81 \pm 0.49 [2.0-6.6]$ |
| Rheumatoid factor, IU/mL ^b | 10.00 ± 0.00 [10.0-3,206.3] | $10.00 \pm 0.00 [10.0 - 3,206.3]$ | 10.00 ± 0.00 [10.0-1,009.4] |
| < 14, No. (%) | 7,623 (92.4) | 3,740 (92.9) | 3,883 (91.9) |
| ≥ 14, No. (%) | 625 (7.6) | 285 (7.1) | 340 (8.1) |
| Total bilirubin, mg/dL | 0.51 (0.38-0.70) [0.10-4.82] | 0.58 (0.43-0.78) [0.10-4.82] | 0.46 (0.34-0.61) [0.10-2.88] |
| Total protein, g/dL | $7.42 \pm 0.40 [3.5 - 9.1]$ | $7.41 \pm 0.41 [3.5 - 8.9]$ | $7.43 \pm 0.40 [6.0-9.1]$ |
| Uric acid, mg/dL | $5.03 \pm 1.41 [0.5-13.3]$ | $5.82 \pm 1.34 [0.9 13.3]$ | $4.28 \pm 1.01 [0.5-9.9]$ |
| UIBC, μg/dL | 213.88 ± 69.35 [5-548] | 194.57 ± 63.66 [5-545] | 232.27 ± 69.55 [10-548] |
| Vitamin B12, pg/mL | 640.00 (508.00-808.00) [50-55,920] | 580.00 (467.00-730.00) [50-9,666] | 697.00 (555.00-875.00) [56-55,920] |
| Vitamin D, ng/mL ^a | 18.69 ± 7.86 [2.7-68.8] | $19.62 \pm 7.56 [2.7-63.9]$ | 17.75 ± 8.05 [3.7-68.8] |

Data are presented as mean \pm standard deviation or interquartile range (Q1-Q3) [min-max].

(48.8%), and the average age was 47.4 years. Of the 26 biomarkers, C-peptide, C-telopeptide of collagen, osteocalcin, and vitamin D were measured in 5,180 participants (2,615 male and 2,565 female). The average of apolipoprotein A1, apolipoprotein B, lipoprotein(a), and high-sensitivity C-reactive protein were 148.2 mg/dL, 102.3 mg/dL, 15.0 mg/dL, and 1.3 mg/L, respectively. In terms of sex differences, women had higher average levels of apolipoprotein A1 and lipoprotein (a), while men had higher average levels of apolipoprotein B and high-sensitivity C-reactive protein. At a cutoff level of 14 IU/mL for rheumatoid factor, 7.6% of participants tested positive. Summary statistics for participants aged 19 years or older for the relevant information are presented in **Supplementary Table 4**.

Research projects derived from the KNHANES biobank project

As of October 17, 2024, a total of 61 projects have been approved, covering a wide range of topics: genetic variants analysis, prevalence research, development of prediction models, and the establishment of clinical reference value (**Fig. 1**). Among the 61 projects, 34 (55.7%) projects included extracted DNA or genotyped data. Yoo et al.¹⁰ reported that alcohol consumption and genetic variants in *CETP* or *ALDH2* affect cholesterol levels. In a study by Kwak et al.,¹¹ genotypes of five SNPs associated with 25(OH)D were analyzed in DNA samples and associations with blood pressure were assessed using mendelian randomization. In the field of prevalence studies, numerous investigations have focused on assessing the seropositivity rates of infectious diseases such as hepatitis A, measles, Japanese encephalitis, and rubella.

 $hs\text{-}CRP = high\text{-}sensitivity \ C\text{-}reactive \ protein, \ UIBC = unsaturated \ iron \ binding \ capacity.$

[°]C-peptide, CTx, osteocalcin, and vitamin D were measured in 5,180 participants (2,615 male and 2,565 female participants).

^bRheumatoid factors were measured using the Roche COBAS Rheumatoid Factors II assay on the Roche COBAS c702 module. The lowest analytical value is 10 IU/mL, and the reference range for negativity is less than 14 IU/mL according to the manufacturer's guidelines.



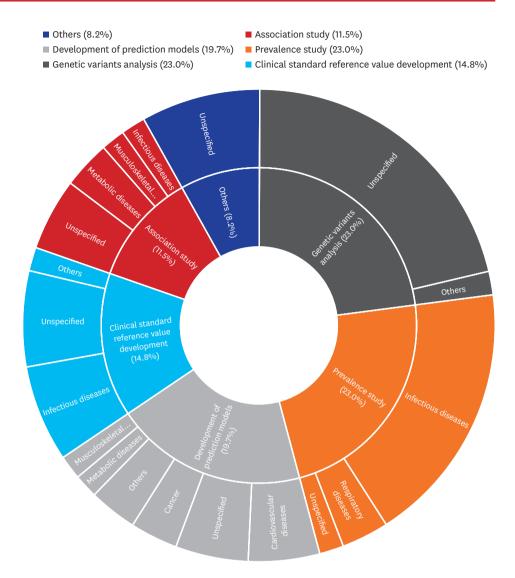


Fig. 1. Sunburst chart of research project types and disease categories approved by the Korea National Health and Nutrition Examination Survey biobank project. The inner ring categorizes studies according to their research objectives, and the outer ring represents the types of diseases studied.

Kim et al.¹² reported national seroprevalence of severe fever with thrombocytopenia syndrome and evaluated regional differences using serum collected from the 2014–2015 KNHANES. In the area of prediction model development, studies have focused on creating polygenic risk scores and personalized models to enable the early identification of high-risk groups for chronic diseases and cancer. Additionally, to establish clinical reference values for Korean women, a project on the 'Reference range for anti-Müllerian hormone testing using automated reagents in healthy Korean women' was conducted using biospecimens provided through this biobank.¹³

This resource enables comprehensive research by linking epidemiologic, laboratory, and genetic data. It supports gene—environment interaction studies (e.g., effects of smoking and genetic variants on lung function), Mendelian randomization analyses using KoreanChip variants to explore causal links between biomarkers and chronic diseases, and nutritional biomarker discovery through integration of dietary recall, blood metabolites, and genetic profiles.



STRENGTHS AND WEAKNESSES

The KNHANES biobank offers a valuable resource of biospecimens of the Korean population. To understand health problems in children and adolescents, resources for biospecimens from general children and adolescents also may be utilized. By allowing a wide range of epidemiological data to be used together, it is possible to gain insight into the detailed nature of health problems. In hospital-based biobanking studies, bioresources from this populationbased biobank can serve as controls. 14 However, several considerations should be kept in mind when utilizing the resource. Owing to the voluntary participation of research participants, the sample size of this national biobank differs from that of KNHANES; however, this gap has been gradually narrowing in recent years. Although there are human biospecimens accumulated over many years, they may not be suitable for studying rare conditions. The KNHANES is a cross-sectional study design that can assess temporary health, nutrition, and lifestyle status, and it is not a longitudinal study, so it is limited in explaining causality. However, the KNHANES plans to establish a cohort for follow-up surveys starting with the 10th cycle survey in 2025, ¹⁵ so these limitations are expected to be resolved. Additionally, the scope of the survey contents, including clinical laboratory measures, may vary from year to year in KNHNES depending on public health considerations. For example, thyroid disease-related tests such as thyroid stimulating hormone, free thyroxine, thyroid peroxidase antibodies, and urinary iodine were measured only in the 6th cycle of KNHANES. Serum vitamin A, vitamin E, and folic acid were measured only in the 7th survey cycle of the KNHNES. The availability of biospecimens varies by type, and since KoreanChip genotyping data from the 8th cycle are not provided for all participants, researchers should verify the latest available resources before planning their research. Currently, data can only be analyzed at the official analysis center. While recalibrated survey weights are not available, limiting direct national representativeness, this resource remains valuable for population-based research. Future efforts to develop recalibrated weights will further enhance its utility.

DATA ACCESSIBILITY

The KNHANES biobank project makes biospecimens available only for approved research studies by their respective Institutional Review Board (IRB). The stored biospecimens are distributed to researchers after review by the NBK Access and Sharing Committee (consisting of approximately 15 committee members including one chairperson). Regular review is held on average once a month to assess the scientific significance and ethical aspects of research for public health. The NBK Access and Sharing Committee is operated fairly and transparently in accordance with the 'Operation and Management Guidelines of the National Biobank of Korea.'

Researchers submit their applications for distribution through the NBK's online platform (HuBIS_Desk, https://biobank.nih.go.kr/Desk/), and can directly contact the coordinator for inquiries regarding the application process. The application can be completed directly online, and must include the following documents: bioresources utilization proposal, agreement, personal information consent form, research proposal (free format), and IRB review result (free format). After the application is approved by the NBK Access and Sharing Committee, the biospecimens are transfer to the researcher after a preparation period of approximately one to three months. Researchers pay fees associated with the distribution of biospecimens, which include sample processing costs (Fig. 2).



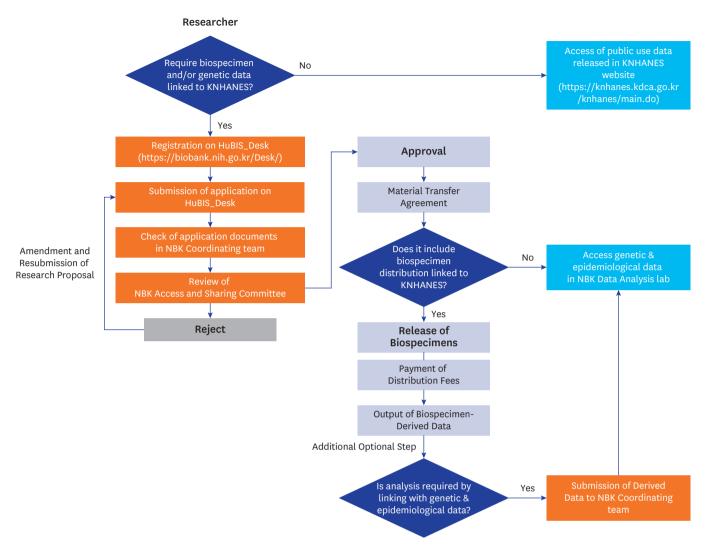


Fig. 2. Flowchart of access for bioresources available in the KNHANES biobank project. KNHANES = Korea National Health and Nutrition Examination Survey.

Currently, data analysis related to the KNHANES biobank can only be accessed in a closed network environment for security reasons at the official analysis center (i.e., NBK Data Analysis lab) located within the Korea Disease Control and Prevention Agency. Therefore, researchers must submit data derived from biospecimens to the NBK Coordinating Team for data analysis procedure. Alternatives are being prepared to improve data accessibility for researchers.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1

The scale of clinical-epidemiological data by survey cycle

Supplementary Table 2

The items of anthropometric and clinical data by survey cycle

Supplementary Table 3

Measurement principles and equipment information for 26 clinical biomarkers

Supplementary Table 4

Summary statistics for 26 clinical biomarkers in adults (aged 19+)

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