

Occupational Noise Exposure and Diabetes Mellitus: A 3-year Retrospective Multicenter Cohort Study

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Abstract

The global prevalence of diabetes has been increasing. However, occupational environmental factors influencing it have been poorly studied. The effect of occupational noise exposure on diabetes is somewhat controversial. Thus, this study examines the relationship between occupational noise exposure (≥ 85 dBA) and diabetes incidence. Participants ($n = 58,284$) were recruited from a Common Data Model cohort of two hospitals from 2013 or 2014 and were annually followed up for three years. Drug history, clinical history of diabetes, and/or fasting glucose of 126 mg/dL or more were defined as new-onset diabetes. Multivariable time-dependent Cox proportional hazard models and Landmark analysis were implemented to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Pooled HRs and 95% CIs were calculated using the weight obtained through standard error. Of the participants, 4.65% developed diabetes during the follow-up. The final adjusted pooled HR of Cox models indicated a significant relationship between occupational noise exposure and increased risk of diabetes (Time-dependent Cox: HR 1.35 [95% CI 1.17–1.57]; Landmark: HR 1.22 [95% CI 1.10–1.35]). There is a significant relationship between occupational noise exposure and incidence of diabetes. Screening for diabetes, active management, and prevention may be necessary to improve the health of individuals exposed to occupational noise.

1 Introduction

Diabetes is a globally prevalent disease that is rapidly increasing because of aging and related lifestyle changes^{1,2}. Over the past 30 years, the number of people diagnosed with diabetes has more than doubled³, and its prevalence was estimated to be approximately 9.3% of the entire global population, which is more than 460 million people⁴. This number may increase to approximately 700 million by 2045⁴. Many studies have elucidated that diabetes is associated with several chronic complications, including ischemic heart disease, stroke, peripheral neuropathy, chronic kidney disease, and heart failure^{5–7}. Furthermore, diabetes can increase mortality from cardiovascular disease (CVD), which is the leading cause of death in most countries worldwide⁸. In the United States, the total estimated national medical expenditure related to diabetes increased from \$188 billion to \$237.3 billion between 2012 and 2017. More than 25% of the total estimated medical expenditure associated with diabetes was attributed to the working population. These costs were associated with absenteeism, presenteeism, productivity losses, work disability, and premature mortality⁹.

Given the length of time most workers spend at their workplace, the working environment may be considered a potential influence or hindrance in the management of diabetes. There are several occupational contributors that increase the risk of developing diabetes, such as sedentary work, limited physical activity, shift work, inadequate time to rest between shifts schedules, and task stressors^{10,11}. Other occupational environmental risk factors such as exposure to noise, heavy metals, and heat are relatively less studied; however, these should be considered as risk factors in the working environment^{12,13}.

Noise is an undesirable sound and is one of the most common environmental stressors present in every human activity. It can be divided into environmental and occupational noise. Occupational noise is more severe than noise in the general environment. The National Institute for Occupational Safety and Health (NIOSH) and American Conference of Governmental Industrial Hygienists (ACGIH) established a permissible noise exposure level to prevent excessive exposure in the workplace. Despite the institutions' recommendation that workers should not be exposed to noise above 85 dBA as per the time-weighted average (equal to the sum of the portion of an 8-hour work shift)^{14,15}, approximately 22.4 million United States workers (17.2%) face occupational noise hazards in their workplace¹⁶. In a European survey, 27% of workers reported that for a quarter of the time or more, they would have to raise their voices to hold a conversation (corresponds to approximately 85–90 dB) due to loud noise in the workplace¹⁷.

Excessive noise exposure remains an occupational hazard worldwide. Previous research suggests that chronic exposure to noise continuously stimulates human organs. This leads to health hazards including cardiovascular diseases, hearing loss, cognitive dysfunction, and sleep disturbances^{18–21}. Previously published literature has established a significant association between environmental noise pollution and diabetes^{22–24}. However, few studies have addressed the association between occupational noise exposure and diabetes. Moreover, these cross-sectional studies demonstrated inconsistent results^{23,25–27}. Conducting further studies that clarify the temporal relationship between occupational noise and diabetes is imperative.

This study aims to bridge this research gap by elucidating the relationship between occupational (≥ 85 dBA) noise exposure and diabetes using three-year follow-up health examination data in Korea with the Common Data Model (CDM) method. It was hypothesized that there would be a significant relationship between the two variables.

2 Method

2.1 Data set

Data from participants who were examined at two hospitals were used from the baseline in 2013 or 2014. The index date was set to the baseline health examination of each participant. Participants underwent annual health examinations until 2016 or 2017 (maximum 3 years), unless otherwise noted. For each health examination, clinical/drug history and abnormal symptoms of participants were surveyed. Factors affecting occupational exposure, including noise, were investigated, and health abnormalities were identified through blood tests during each annual health examination.

Severance Hospital and Ulsan University Hospital established a Korea Workers Health Examination Common Data Model (KWHE-CDM) based on worker health examination data. KWHE-CDM is a distributed CDM, a method for standardizing data amongst diverse local database systems. Most variables were matched with Nebraska Lexicon, Systematized Nomenclature of Medicine-Clinical Terms, and Logical Observation Identifiers Names and Codes, which are standard vocabulary terms in

Observational Medical Outcomes Partnership CDM²⁸. Questionnaires that were not matched to the standard vocabulary terms were defined using KWHE-defined coding. The distributed CDM allowed data to have the same coding and structure, allowing each institution to run the same analysis independently.

Initially, all workers with baseline health examination data were included in the study (Severance Hospital: n = 24,370, Ulsan University Hospital: n = 60,743). Subsequently, participants in companies where all workers were not exposed to occupational noise exposure (Severance Hospital: n = 2,358, Ulsan University Hospital: n = 9,858), workers who were not followed up for any health examination until 2017 (Severance Hospital: n = 4,258, Ulsan University Hospital: n = 7,023), and workers who reported that they have been diagnosed with diabetes mellitus or take medication for diabetes mellitus, or who have a fasting blood glucose of 126 or higher at the time of the baseline examination (Severance Hospital: n = 1,035, Ulsan University Hospital: n = 2,297) were excluded. After exclusion, 16,719 workers in Severance Hospital and 41,565 workers in Ulsan University Hospital were finally enrolled in the current study.

2.2 Outcomes and variables

The primary outcome of this study was to determine the incidence of diabetes among participants. Presence of diabetes was indicated if participants were diagnosed with diabetes mellitus, took medication for diabetes mellitus, or had a fasting blood glucose of 126 or higher at the time of the baseline examination. Blood glucose was measured through a blood test, not Point of Care Testing, and was performed by a trained nurse for each health examination. All participants were required to fast overnight prior to drawing blood during the health examinations.

Occupational noise exposure, which is the first independent variable, was defined based on the criteria of Threshold Limit Values (TLV) provided by ACGIH, depending on whether or not the worker was exposed to noise at 85 dBA or more for 8 hours during work¹⁵. The Korean government announced Article 125 (Working Environment Monitoring), which require government-certificated industrial hygienists to visit the workplace and conduct a walk-through survey with workers and related officers using interviews²⁹. Noise levels in the work environment are measured in dBA, using a sound level meter conforming to the requirements of the American National Standards Institute Sound Level meters. Information about whether participants were exposed to noise or not in each health examination were extracted from the CDM exposure database.

Covariates were obtained from self-reported questionnaires and measurements of health examination. Participants responded to a question on smoking: "Have you smoked 100 cigarettes or more in your lifetime?" Based on the responses and current smoking status, participants were grouped as non-smokers, past-smokers, and current-smokers. According to Asian guidelines for obesity, Body Mass Index (BMI) was categorized as follows: underweight (<18.5), normal (18.5–22.9), overweight (23–24.9), and obese (≥ 25)³⁰. Male participants who reported drinking more than seven drinks per week, and female participants who reported drinking more than five drinks per week, were classified as having a history of drinking. Others were classified as not having a history of drinking. Hypertension among participants was defined based on a diagnosis of hypertension, intake of medicines to control hypertension, and systolic

blood pressure of 140 or higher or diastolic blood pressure of 90 or higher. Blood pressure was measured by qualified nurses using an automated blood pressure monitor. If blood pressure was found to be too high, participants rested for 10 minutes before taking another reading. Participants were grouped based on physical activity: an exercise group that undertook high- or medium-intensity exercise more than twice a week, and a non-exercise group who did not.

In South Korea, chemical exposures—such as to carbon monoxide, nitric oxide, cyanide compounds, antimony compounds, carbon disulfide, trichloroethylene, ethylene glycol dinitrate, acetonitrile, methyl chloroform, dichlorofluoromethane, dichloromethane, and nitroglycerin—and physical exposure, such as vibration, high- or low-pressure, and night shift, are classified as risk factors for CVD by the Korean Occupational Safety and Health Act.³¹ As a result, we identified cardiovascular-related exposure among participants with any of those factors. Further, number of cardiovascular-related exposure per participant was calculated and used as an adjusting variable. Moreover, experts that specialize in evaluating the work environment, examined all cardiovascular-related hazards.

2.3 Statistical analysis

For continuous and categorical data, independent t-tests and chi-squared tests were used to examine differences between baseline health examination data of participants with and without occupational noise exposure. As illustrated in Table 1, which includes the baseline characteristics, participants who were exposed to noise within any period of follow-up were considered as the noise exposure group.

Table 1
baseline characteristics of participants by severe noise exposure

Variable	Non-Exposure	Noise Exposure	p-value
Age			<0.001
Mean (SD)	39.22 (9.91)	44.91 (10.21)	
Sex			<0.001
Male	19077 (65.13%)	27907 (96.25%)	
Female	10214 (34.87%)	1086 (3.75%)	
Hypertension			<0.001
No	26125 (89.19%)	25202 (86.92%)	
Yes	3166 (10.81%)	3791 (13.08%)	
Smoking history			<0.001
non-smoker	16531 (56.44%)	7700 (26.56%)	
ex-smoker	5715 (19.51%)	8367 (28.86%)	
current-smoker	7045 (24.05%)	12926 (44.58%)	
Body Mass Index			<0.001
underweight	1635 (5.58%)	282 (0.97%)	
normal	12906 (44.06%)	11223 (38.71%)	
overweight	6974 (23.81%)	8840 (30.49%)	
obese	7776 (26.55%)	8648 (29.83%)	
Drinking History			<0.001
No	17749 (60.60%)	12996 (44.82%)	
Yes	11542 (39.40%)	15997 (55.18%)	
Exercise History			<0.001
No	9644 (32.92%)	4386 (15.13%)	
Yes	19647 (67.08%)	24607 (84.87%)	
Presence of Cardiovascular-related Exposure			<0.001
No	25270 (86.27%)	12036 (41.51%)	
Yes	4021 (13.73%)	16957 (58.49%)	
Diabetes (Outcome)			<0.001

Variable	Non-Exposure	Noise Exposure	p-value
No	28236 (96.40%)	27336 (94.28%)	
Yes	1055 (3.60%)	1657 (5.72%)	

The duration from the moment of occupational noise exposure to diabetes incidence was plotted using the Kaplan-Meier method. Using a multivariable time-dependent Cox proportional hazard model to adjust for the immortal time bias, hazard ratios (HRs) with 95% confidence intervals (CIs) of diabetes incidence were estimated³². Each participants' health examination data and the time intervals between health examinations were used in time-dependent Cox analysis. Landmark analysis with time-fixed Cox proportional hazard models, a method to reduce the immortal time bias, were further performed as a sensitivity analysis³³. Landmark period was set to one year, which implies that participants exposed to noise within 1 year after the index date were classified as the noise exposure group and participants who were diagnosed with diabetes within 1 year after the index date were excluded.

The same statistical method was performed in both cohorts according to the distributed CDM method. Pooled HRs and 95% CIs of hypertension were calculated using the weight obtained through standard error. All statistical tests were two-tailed and statistical significance was defined as a p-value of less than 0.05. All statistical analyses were carried out with R version 4.0.3's "survival" packages (R Foundation for Statistical Computing, Vienna, Austria).

2.4 Ethics statement

The study protocol was approved by the Institutional Review Board of Severance Hospital (IRB: Y-2020-0011) and Ulsan University Hospital (IRB: 2020-03-043), and followed the ethical requirements of the 1975 Declaration of Helsinki. As this study is retrospective in nature, informed consent from the participants was waived by Institutional Review Board of Severance and Ulsan University Hospital.

3 Results

Table 1 summarizes baseline characteristics of participants stratified by occupational noise exposure in both hospitals. The mean age and standard deviation (SD) of total participants were 42.05 and 10.27, respectively. Of the participants, 46,984 (80.6%) were male. The noise exposure group was significantly older (M = 44.91, SD = 10.21, $p < 0.001$) compared with the non-exposure group (M = 39.22, SD = 9.91). Of the participants, 2,712 (4.65%) developed diabetes during the follow-up period: 5.72% in the noise exposure group and 3.60% in the non-exposure group. Occupational noise exposure was six times more prevalent among male participants (59.40%) compared with their female counterparts (9.61%). The number of cardiovascular-related exposures, hypertension, smoking history, higher BMI, age, drinking history, and exercise history, was significantly more prevalent in the noise exposure group ($p < 0.001$). The baseline characteristics of each participant in the two hospitals are summarized in Supplementary Table S1. Baseline characteristics of participants at each hospital yielded a similar trend to that of the total

cohort, except that exercise history was not significantly different between both groups in Ulsan University Hospital.

Kaplan-Meier plots of the proportion of diabetes development among participants in each hospital are shown in Figure 1a and 1b (1a: Severance Hospital, 1b: Ulsan University Hospital). Both hospitals show significant difference in the incidence of diabetes between noise exposure and non-exposure groups ($p < 0.0001$).

Table 2 summarizes the HRs and 95% CIs of diabetes, based on occupational noise exposure in each hospital cohort and pooled cohort. The association between occupational noise exposure and the increased risk of diabetes was significant in each cohort for time-dependent Cox and Landmark analysis, respectively. Both analyses were adjusted with equivalent sequence of covariates. Model 1 was adjusted using age and sex. Smoking history, BMI, and drinking history were added as covariates in Model 2. Finally, Model 3 was further adjusted with hypertension, exercise history, and the number of exposures related to cardiovascular risk. All models, from the crude model to the final model, showed statistical significance.

Table 2
Hazard Ratios and 95% Confidence Intervals of diabetes by severe noise exposure

		crude model	model 1 ^a	model 2 ^b	final model
Time dependent	Severance Hospital	2.67 (2.24-3.20)	1.52 (1.26-1.84)	1.49 (1.24-1.80)	1.50 (1.23-1.81)
	Ulsan	1.72 (1.56-1.88)	1.30 (1.18-1.43)	1.33 (1.21-1.47)	1.28 (1.15-1.43)
	Total	2.13 (1.38-3.28)	1.38 (1.19-1.59)	1.37 (1.25-1.50)	1.35 (1.17-1.57)
Landmark	Severance Hospital	2.27 (1.87-2.75)	1.30 (1.06-1.59)	1.29 (1.06-1.58)	1.28 (1.04-1.56)
	Ulsan	1.61 (1.45-1.78)	1.23 (1.11-1.37)	1.25 (1.13-1.39)	1.20 (1.07-1.35)
	Total	1.89 (1.35-2.65)	1.25 (1.14-1.37)	1.26 (1.15-1.38)	1.22 (1.10-1.35)
a: adjusted by age and sex					
b: adjusted by age, sex, smoking history, body mass index, and drinking history					

Pooled HRs of time-dependent Cox and Landmark analyses revealed a significant association between occupational noise exposure and incidence of diabetes (Time-dependent Cox: HR 1.35 [95% CI 1.17–1.57]; Landmark: 1.22 [95% CI 1.10–1.35]). Older age, male sex, a current-smoker, overweight and obesity, drinking history, and hypertension were significantly correlated with increased risk of diabetes in time-

dependent Cox models of the pooled cohort. Older age, male sex, overweight and obesity, drinking history, hypertension, and the number of exposures related to cardiovascular risk were significantly relevant to increased risk of diabetes in the Landmark analysis of the pooled cohort. Detailed contents of models of both hospitals are presented in supplementary Table S2 (Time-dependent Cox models), supplementary Table S3 (Landmark analysis models), and supplementary Table S4 (Pooled models).

4 Discussion

This study reveals that occupational noise exposure increases the risk of diabetes incidence. This relationship was significant in time-dependent Cox models of two hospital cohorts, as well as the pooled cohort. All models in each group showed statistical significance in terms of the relationship between occupational noise exposure and diabetes. The relationship was significant even after adjusting for potential confounding variables. Further, a Landmark analysis, a method to reduce immortal time bias, was performed as a sensitivity analysis, and the results showed a statistically significant relationship between occupational noise exposure and increased risk of diabetes.

Our time-dependent Cox and Landmark analysis models adjusted for several covariates that are established risk factors of diabetes. This includes demographic factors (age and sex), lifestyle factors (BMI, smoking, exercise, and drinking alcohol), and clinical history (hypertension)^{34–36}. Furthermore, by adjusting for factors of cardiovascular-related exposure, in addition to the existing commonly known variables, it was possible to reduce the bias caused by exposure from various work environments.

There have been several studies that elucidate the relationship between lifestyle factors and improvement of diabetes symptoms. A strategy such as the Diabetes Prevention Program (DPP) in the workplace, for prevention of type 2 diabetes mellitus was promoted to manage costs and improve population health³⁷. In 2002, the DPP research group demonstrated that a 7% body weight loss and 150 minutes of physical activity per week could reduce a three-year incidence of type 2 diabetes mellitus among people with prediabetes, by 58%³⁷. The DPP lifestyle intervention has since been developed into a year-long, group-based program that helps people lose weight in a variety of clinical settings^{38,39}. However, there is insufficient research on occupational environmental factors of diabetes, compared with lifestyle factors, and intervention research is especially lacking. Intervention studies on preventing occupational noise exposure have been focused on hearing loss⁴⁰. Considering that a lot of workers are exposed to occupational noise¹⁶, policies for improving the health impacts of those workers are imperative. The strong relationship between diabetes and occupational noise exposure demonstrated in this study contributes to the recognition of occupational environmental factors as an important risk factor in diabetes incidence. Future studies focused on policies and protection guidelines should be implemented.

Several studies have elucidated the association between severe occupational noise exposure and diabetes; however, their results were mostly negative, and they had limitations. Dzhambov (2017) conducted a cross-sectional study with the 7th European Social Survey and showed a non-significant result of the relationship between occupational noise exposure and diabetes (Odds ratio (OR) 1.01 [95%

CI 0.78–1.32])²⁵. However, in this study, noise exposure was defined as being exposed to a very loud noise even once, which is less accurate for stratifying noise exposure. Dzhambov (2015) also conducted a meta-analysis of long-term noise exposure and the risk for diabetes. Occupational noise exposure studies yielded insignificant results of relative risk of diabetes (pooled effect 1.12 [95% CI 0.95–1.31]); however, those studies were cross-sectional or restricted to a specific sex²³.

In contrast, Chang et al. (2020) conducted a retrospective cohort study of 905 industry-based workers. The study showed a significant relationship between occupational noise exposure and incident hyperglycemia (Relative Risk 1.80 [95% CI 1.04–3.10])²⁷. However, this study focused on hyperglycemia—which includes impaired fasting glucose—and did not reflect co-exposure factors and time-varying lifestyle factors. The current study supplemented the limitations of previous studies by using time-dependent Cox models and reduced bias in various ways.

In terms of potential mechanism, noise exposure could be a risk factor for diabetes by significantly affecting stress or sleep. Noise increases catecholamine synthesis, resulting in insulin resistance and problems with glucose homeostasis, thereby increasing stress^{41,42}. Furthermore, noise exposure could result in sleep disturbances, which cause irregular blood glucose and increase in adiposity⁴³. According to these theories, just as environmental noise exposure is related to diabetes, severe occupational noise exposure is also considered to have some degree of correlation.

The current study has several strengths. First, various methods were applied to overcome the immortal time bias. A multivariable time-dependent Cox proportional hazard analysis was performed and reflected the variability of lifestyle factors and BMI. The Landmark analysis was also implemented for sensitivity analysis and indicated the same trend of results. Second, using the same statistical method analysis, two hospital cohorts in different regions were included, so that the data showed diversity and could minimize bias caused by specific regions or institutions. This distributed CDM method could result in a larger sample size by applying the same statistical syntax on different data while maintaining the security of data. Third, to reduce selection bias, the participants of companies with occupational noise exposure were enrolled and noise exposure and non-exposure groups in those companies were compared with each other. Finally, the models were adjusted with number of exposures related to cardiovascular risk, which was not considered in previous studies, along with well-known risk factors of diabetes (demographic characteristics and lifestyle factors).

However, there are some limitations due to the incompleteness of health examination data. First, the health worker effect could influence the outcome of the current study. This implies that healthier workers survive in the company so that they could be more exposed to harmful factors. The maximum follow-up period was set at three years, which is not exceedingly long, to reduce the health worker effect. Moreover, diabetes is less severe than, for example, cancer or CVD, which implies less probability of retirement due to the disease outcome.

Second, some factors such as hearing disease history, disease treated with high-dose steroids, and the presence of personal protective equipment, which could affect diabetes, were not included in our study. Moreover, information about participants' previous occupational environment was unclear. Further well-designed studies that overcome this limitation should be implemented.

Third, the exact date participants were diagnosed with diabetes is unclear since the definition of diabetes outcome was based on the questionnaires and fasting blood glucose. Thus, the follow-up period may have a bias. Nonetheless, hypertension and diabetes are often found incidentally in health examinations, rather than diseases that are diagnosed by visiting a hospital due to severe symptoms. Moreover, although the time of diagnosis is not clear in the case of history of high blood pressure, diabetes, or taking medicine, the degree of duration will be spread randomly between noise exposure group and non-exposure group. Thus, this limitation can be overcome. Lastly, noise exposure was not quantified in this study. However, the occupational noise standard of 85 dBA lasting 8 hours or more suggested by the ACGIH was applied. Therefore, it is meaningful to evaluate the health effects of workers exposed to serious severe noise. It is also meaningful to check the dose-relationship through a quantitative noise exposure data cohort in the future.

In conclusion, there is a significant association between occupational noise exposure and increased risk of diabetes. Screening for diabetes, active management, and prevention are necessary to improve the health of numerous individuals exposed to occupational noise.

Declarations

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Conflicts of Interests

None.

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Author Contributions

Conceived and designed the study: B.Yun, J.Sim, and J-H.Yoon; Analysed the data: B.Yun, J.Sim, J-H.Yoon, and C.Kim; Visualization: A.Cho, S.Kim, and B.Yun; Validation: J.Sim and C.Kim; Investigation: J.Oh, S.Kim, and Y.Oh; Contributed analysis tools: C.Kim, Y.Oh, and S.Lee; Wrote the paper: B.Yun, J.Oh,

J.Sim, and S.Kim; Revised the manuscript: J.Lee, S.Lee and J-H.Yoon. All authors have reviewed the manuscript.

Data Availability

The datasets generated during and/or analysed during the current study are not publicly available due to the privacy of the hospital data.

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Figures

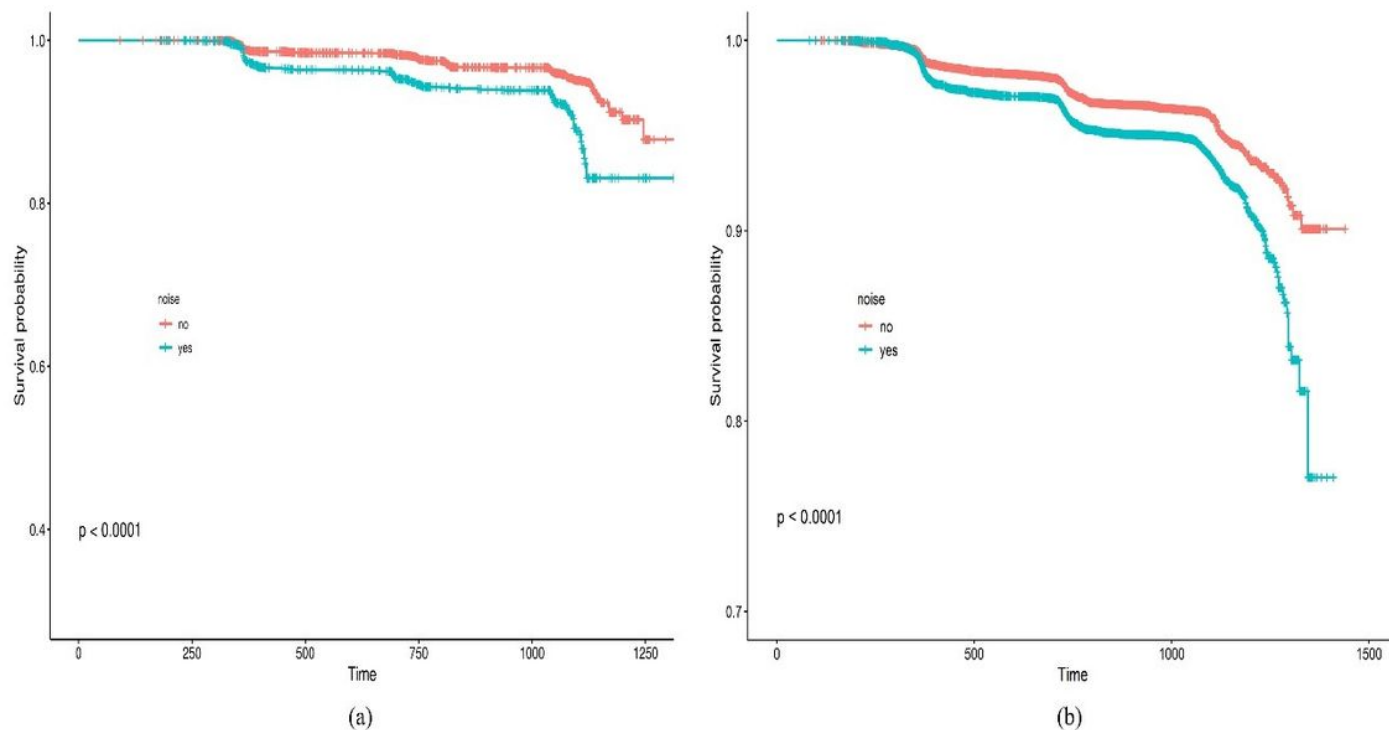


Figure 1

Kaplan-Meier plots of the proportion of diabetes development among participants in the two hospitals (a) Severance Hospital (b) Ulsan University Hospital

Supplementary Files

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