Ann. N.Y. Acad. Sci. ISSN 0077-8923

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Special Issue: Annals *Reports*

Original Article

Medical phenome of musicians: an investigation of health records collected on 9803 musically active individuals

Maria Niarchou,[1] George T. Lin,[2] Miriam D. Lense,[3,4] Reyna L. Gordon,[1,3,4] and Lea K. Davis[1,5,6,7,8]

[1]Vanderbilt Genetics Institute, Vanderbilt University Medical Center, Nashville, Tennessee. [2]Vanderbilt University School of Medicine, Nashville, Tennessee. [3]Department of Otolaryngology – Head & Neck Surgery, Vanderbilt University Medical Center, Nashville, Tennessee. [4]Department of Psychology, Vanderbilt University, Nashville, Tennessee. [5]Division of Genetic Medicine, Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee. [6]Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, Tennessee. [7]Department of Psychiatry and Behavioral Sciences, Vanderbilt University Medical Center, Nashville, Tennessee. [8]Department of Molecular Physiology and Biophysics, Vanderbilt University, Nashville, Tennessee

Addresses for correspondence: Maria Niarchou and Lea K. Davis, Ph.D., Vanderbilt Genetics Institute, Vanderbilt University Medical Center, Light Hall, 2215 Garland Avenue, Nashville, TN, 37240. maria.niarchou@vumc.org; lea.k.davis@vumc.org; Reyna L. Gordon, Ph.D., Vanderbilt Bill Wilkerson Center, MCE, Nashville, TN, 37232. Reyna.gordon@vanderbilt.edu

Previous studies suggest that musicians may be at higher risk for a set of medical problems; however, this literature has been limited by relatively small sample sizes, self-reports, and lack of controls. To address such limitations, we examined trends in the medical care of musicians in an Electronic Health Record database. On the basis of a collection of keywords and regular expressions in the patients' clinical notes, we identified 9803 "musicians" that we matched for sex, median age (across the medical record), ethnicity, race, the length of record, and the number of visits with 49,015 controls. We fitted 1263 logistic regression models to determine whether the phenotype was correlated with musicianship. Two hundred fifty-seven phenotypes were more prevalent in musicians than controls after Bonferroni adjustment ($P < 7.6 \times 10^{-6}$), including diseases of the larynx and vocal cords (OR = 2.32 (95% CI: 2.25–2.40)), and hearing loss (OR = 1.36 (95% CI: 1.32–1.39)). Fifteen phenotypes were significantly more prevalent in controls than musicians, including coronary atherosclerosis (OR = 0.91 (95% CI: 0.89–0.94)). Although being a musician was related to many occupational health problems, we identified protective effects of musicianship in which certain disorders were less common in musicians than in controls, indicating that active musical engagement could have health benefits analogous to athletic engagement.

Keywords: musicians; electronic health records; PheWAS; physical health problems; mental health problems

Introduction

Similar to elite athletes, musicians undergo years of effortful training and dedicated practice in order to be able to play music at a professional level. The demands associated with the profession are enormous and can impact multiple aspects of a musician's life and health. Lack of financial security and career stability, repeated competitive evaluations, and performance-related demands[1] can be sources of stress, while the physical demands to be able to perform at a high level increase vulnerability to physical injuries (e.g., repetitive use injuries).[2] Despite the challenges associated with this career path, the national infrastructure for professional musicians' health is less robust than services for elite athletes, where sports medicine strategies for improving wellness are the norm,[3] though there are notable exceptions of organizations like MusiCares (https://www.grammy.com/musicares/about) and a relatively small number of highly specialized medical clinics that specialize in musicians' health.

doi: 10.1111/nyas.14671

Studies indicate a variety of physical health problems associated with being a musician, including musculoskeletal[4] (e.g., tendonitis)[5] and skin disorders,[6] respiratory problems,[7] and hearing loss.[2] Mental health problems are also common, including performance-related anxiety,[8] anxiety, depression,[9,10] and sleep problems.[10,11] Alcohol, medication, and drug use are frequently encountered among recording musicians[10,12] despite their known risks and contributions to the premature mortality of famous musicians (e.g., Ref. 13). Adding to these risks, women in the music industry face additional societal obstacles and stressors linked to gender discrimination, lower compensation, challenges with childcare, and balancing family responsibilities, according to a 2019 report.[14] Large-scale data show disparities in how music by female artists is perceived, shared, and promoted.[15] Women music teachers report higher rates of occupation-related pain, such as neck and shoulder pain.[16]

On the other hand, there are well-documented benefits of musical engagement and training, including enhanced well-being and social bonding,[17] executive function and other cognitive tasks,[18,19] and enhanced physical performance during exercise.[20] There is also substantial literature showing that older adult musicians are resilient to some cognitive and speech perception–related effects of age-related hearing loss relative to their nonmusician peers,[21] potentially via training-related neural plasticity. Disentangling causation versus correlation of these relationships between music engagement and health is becoming the focus of many new studies (Ref. 22, also see Ref. 23 as an example of a randomized control trial that could shed light on causation).

The extent of the health risks and benefits of music participation and professional music activities has not yet been studied comprehensively, especially in professional musicians, who are in many ways comparable with professional athletes. For instance, a study of 62 professional musicians indicated that the level of heart rate response during a concert performance was similar to the heart rate response of professional athletes, highlighting the high physiological demands of professional musicianship.[24] Most studies of musicians' health, however, are based on relatively small sample sizes and self-report questionnaire data and often lack control groups. Therefore, our understanding of the scope and prevalence of physical and mental health problems in musicians is limited.

To address the limitations of previous studies, we conducted an extensive study of 86,274 individuals to identify the health disorders for which musicians are more frequently coded, using data from Electronic Health Records (EHRs) in a deidentified research database. Nashville, known as "Music City," has a large population of working musicians, and the Vanderbilt University Medical Center has a reputation for providing specialized medical care to musicians from the Nashville area and beyond, thus improving our statistical power to perform such analyses. Our study examined the following questions: What are the most frequent physical and mental health problems of musicians reported in the EHR compared with a control sample? In light of sex differences in the prevalence of many health problems and that women in music careers may face special environmental and health challenges, are there sex differences observed for any musician-associated health disorders? Given recent advances in phenome-wide association studies (PheWAS) methodologies for epidemiological discovery in data-rich EHR research databases,[25] we employed PheWAS approaches to conduct data-driven exploration in the Vanderbilt patient population. Taking into account that health issues that musicians face can be related to their instrument,[2] we also examined what medical problems are associated with musicians who play different families of instruments (e.g., string and brass instruments and voice). Finally, we also examined the health problems in children and adolescents to explore potential musician-related health problems observed early in life.

Materials and methods

Vanderbilt's EHR database

The study was conducted using the Synthetic Derivative (SD) database at the Vanderbilt University Medical Center (VUMC). The SD is the deidentified version of the entire VUMC Electronic Medical Records system, which contains records of over three million unique individuals.[26] The database incorporates data from multiple components, including diagnostic and procedure codes, demographics, progress and nursing notes, problem lists, and medication histories. This study was approved

Table 1. Keywords for instrument families and descriptives

Keywords					
Main category	Keywords	*N* cases (% males)	*N* controls (% males)	*N* cases, mean age (SD)*	*N* controls, mean age (SD)*
Musician[a]	Musician, songwriter, and all keywords listed below	9803 (58%)	49,015 (60%)	47.8 (17.2)	47.5 (17.4)
Vocalist	Singer and vocalist	2387 (43%)	11,935 (44%)	46.0 (16.5)	44.9 (16.7)
Percussion	Drums, timpani, tambourine, and percussion	886 (84%)	4430 (85%)	43.5 (15.2)	43.2 (16.0)
Keyboards	Piano, keyboards, organ, synthesizer, harpsichord, and accordion	2106 (35%)	10,530 (35%)	54.8 (18.0)	55.9 (17.5)
Brass	Trumpet, trombone, French horn, bass trombone, and tuba	340 (72%)	1700 (74%)	44.8 (19.6)	44.6 (17.4)
Strings	Steel guitar, dobro, viola, cello, ukulele, pedal steel, guitar, bass, mandolin, banjo, fiddle, and violin	3209 (75%)	16,045 (76%)	47.8 (16.5)	46.8 (17.1)
Woodwinds	Clarinet, flute, piccolo, oboe, English horn, bass clarinet, saxophone, and harmonica	482 (39%)	2410 (40%)	41.9 (19.4)	41.4 (16.9)

[a]The musician category includes keywords from all categories.
*Mean median age of the record.

by the Vanderbilt Institutional Review Board for nonhuman subjects research (IRB #160302).

The musician-related keyword selection

We determined the musician status in patient records through keyword searches in patients' deidentified EHRs from the SD database. To generate an initial keyword list, we obtained the number of individuals per instrument type or musician-related profession from the Nashville Musicians Association, the local affiliate of the American Federation of Musicians of the United States and Canada. The initial list included 100 keywords (Table S1, online only). Out of these, we selected the instrument-/music-related professions that were endorsed by more than 10 individuals in the keyword list, which reduced the list to 44 keywords. We then conducted 300 chart reviews (seven charts per keyword) to examine whether the keywords are within context (i.e., whether they characterize individuals who are musicians). As a result of the searches, we removed eight keywords as they mostly captured nonmusician-related traits (e.g., arranger, contractor, copyist, programmer, and recorder (i.e., recording engineer)). Using only the name of the musical instrument returned results for which the keyword was unrelated to music contexts (e.g., bass fishing, accordion drainage bag, mandolin slicer, and banjo curette); thus, we restricted the search to 449 regular expressions (e.g., "play the") plus the name of the musical instrument as a keyword (for details, see Fig. 1, Table 1, and Table S2, online only), and four keywords that were added to the search separately (i.e., songwriter, musician, singer, and vocalist). Here, for simplicity, we use the term *keyword* to refer to both keywords and regular expressions. We also excluded from the search the following phrases as this was the name of a commonly recommended book for children with autism: "The Different Drummer," "the different drummer," "Different Drummer," and "different drummer." We restricted our search to patients for whom VUMC was the most likely source of primary care using a heuristic "medical home" definition (i.e., five codes on different days over 3 years). This approach reduces false-positive associations that could be due to systematic missingness in the data. The final search resulted in 14,927 individuals qualifying as musicians.

Chart reviews

Two reviewers (the authors M.N. and G.L.) each reviewed 10% ($N = 1498$) of randomly selected records from the set of musician cases identified by the keyword search described above to establish the positive predictive value (PPV). Charts were evaluated for evidence of musicianship and did not restrict the search to professional musicians. Individuals were considered as musician cases if

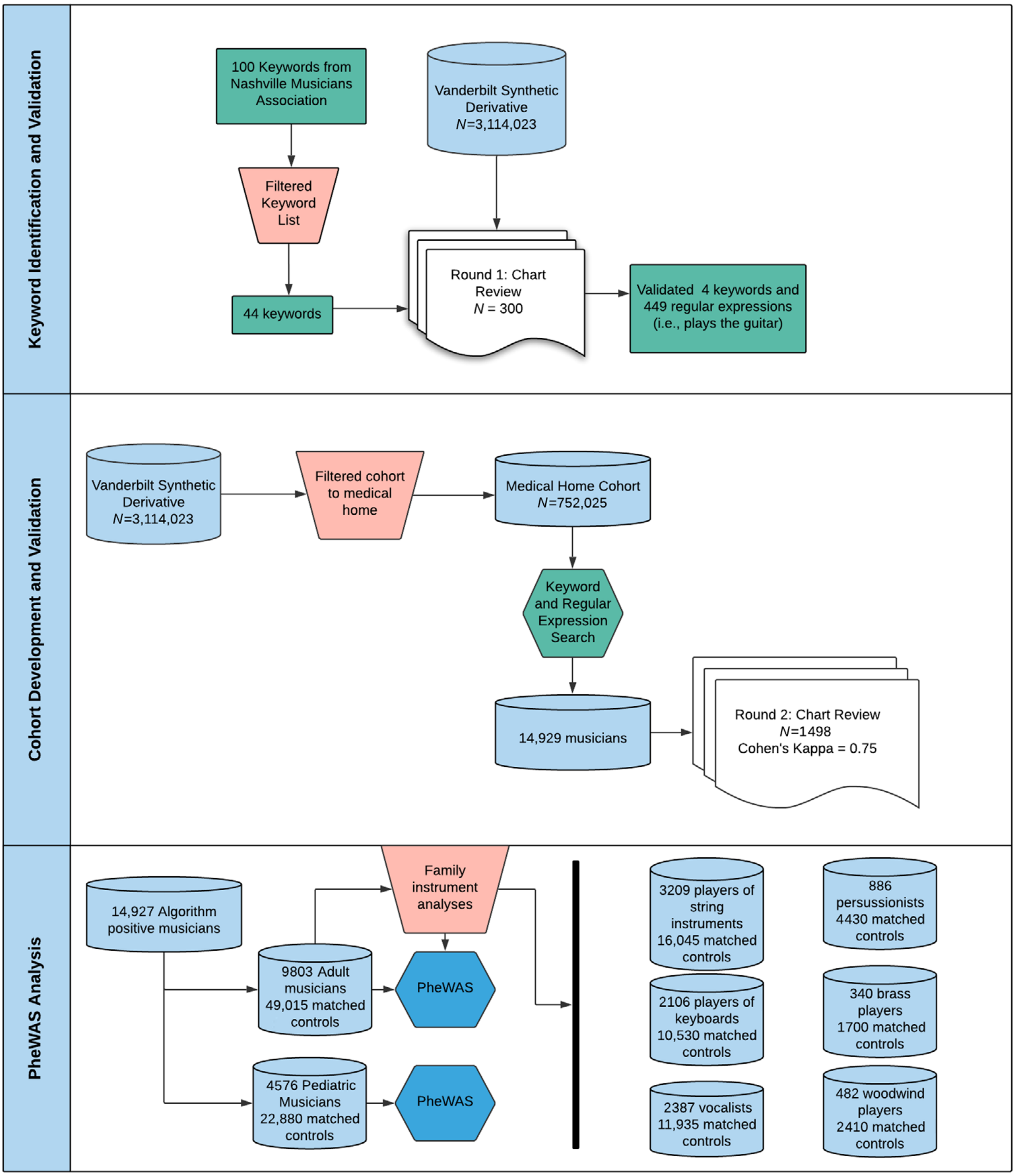

Figure 1. Keyword selection process and chart review. *Keyword identification:* we obtained the initial list of keywords ($n = 100$) from the Nashville Musicians Association. We further reduced the list to 44 keywords by selecting the instruments/music-related professions that were endorsed by more than 10 individuals in the keyword list. We then conducted 300 chart reviews, where we identified and validated four keywords and 449 regular expressions. *Cohort development and validation:* we restricted our search to patients for whom VUMC was their "medical home" (i.e., five codes on different days over 3 years). Using the four keywords and 449 regular expressions identified previously, we identified $n = 14{,}927$ musicians in total. *PheWAS analysis:* out of those, $N = 9803$ had the median age of record > 18 and $N = 4576$ had a median age of record ≤ 18 and ≥ 5. We also separated musicians into groups on the basis of the instrument they were playing. Each group was matched in a 1:5 ratio for the median age and length of record, the number of visits, sex, race, and ethnicity, and a PheWAS was run for every group.

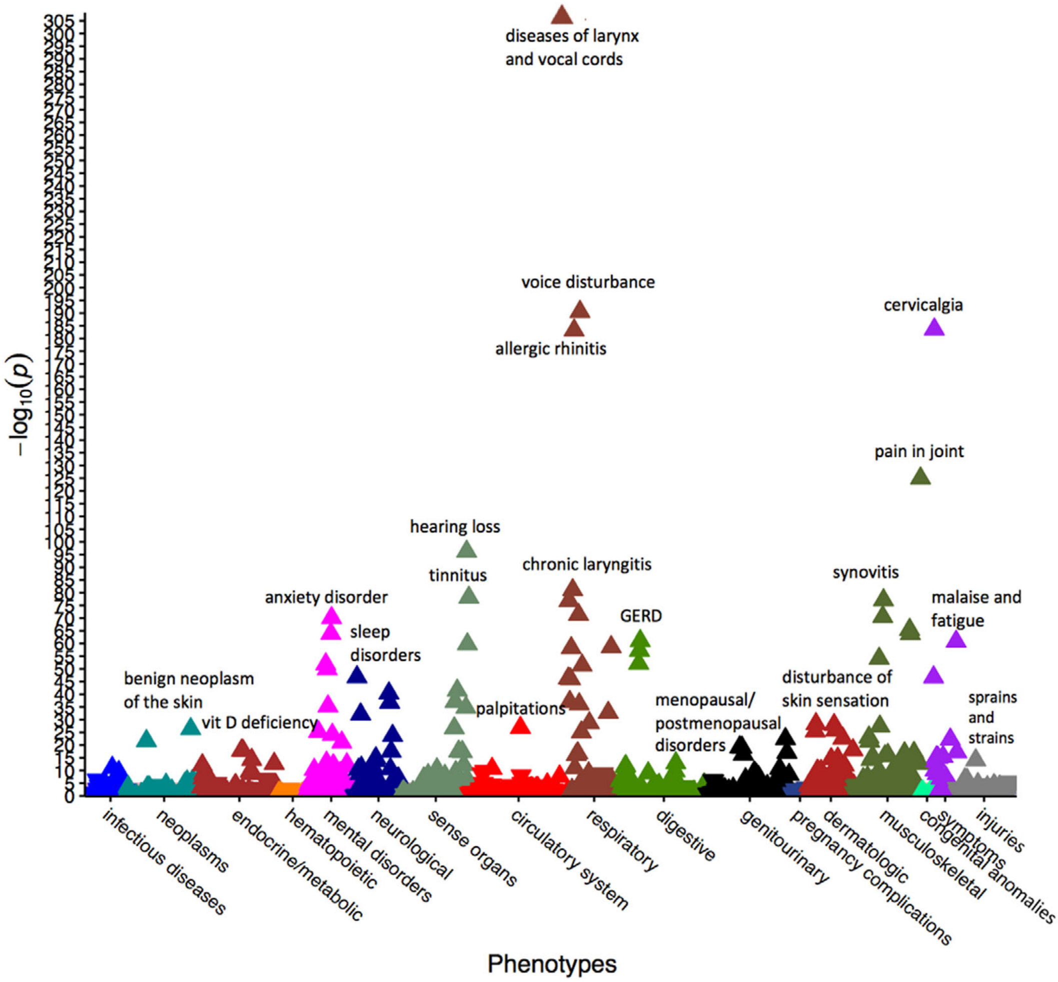

Figure 2. **PheWAS plot of musicians versus control population in the Electronic Health Records. Phecode categories are on the *x*-axis, *P* values ($-\log_{10}$) are on the *y*-axis, and the triangles are the specific phecodes within the phecode categories. If the direction of the effect is positive, the arrows point upward; if the direction of the effect is negative, the arrows point downward.**

their record included evidence that they played a musical instrument or were a musician. The procedure was as follows: each reviewer loaded the record of the individual in the SD interface and searched for the keyword in all the documents of the individual's record. Each author separately read the phrase/paragraph within which this keyword was included and determined whether it was within the context of patient musician activity or not. The reviewer agreement was 97% based on 1498 charts, and Kappa inter-rater reliability was 0.75 (substantial agreement). The approach yielded a high PPV of 93%.

For the control sample (i.e., nonmusicians), we included all individuals who had no mention of musician keywords in their medical charts and matched them to musicians in a ratio of 1:5 for the median age across the medical record, the length of record, the number of visits, sex, race, and ethnicity. We used the R MatchIt package (using the nearest neighbor-matching setting). Control (or nonmusician) charts had no keywords from our initial list. It is possible that some controls include musicians who do not have a record of these keywords in their charts. This type of misclassification (i.e., cases as controls) could result in reduced power but is unlikely to result in increased type 1 error because the longitudinal nature of the EHR provides ample opportunity for occupation-related and -unrelated health concerns to surface. Given our large sample size, the loss of power because of the potential misclassification of cases as controls was not a significant cause of concern for our study.

Statistical analyses

For our primary analyses, we restricted our sample to individuals with a median age of record over 18 years of age. We performed a PheWAS.[27] The PheWAS is based on the phecode system that uses International Classification of Disease versions 9 and 10 (ICD-9 and ICD-10) codes. Specifically, for the development of the phecodes, one or more related ICD-9 and ICD-10 codes were combined into distinct phecode categories (that we refer to as phenotypes in the paper) after consultations from experts in different medical fields.[28] The phecodes have a standardized vocabulary and can refer to conditions, diseases, or symptoms. For our PheWAS, we used the EHR-derived case–control status for 1263 phecodes (phenotypes) and estimated associations with musician status (case versus controls) in Vanderbilt's EHR database. ICD codes were converted to phecodes using the R PheWAS package.[25] The mappings of ICD codes to phecodes can be found here (http://phewascatalog.org). We restricted our analyses to phecodes that had over 100 cases or controls. We also performed supplementary analyses where we adjusted for the median body mass index (BMI) (Table S5, online only). We also repeated the approach to perform exploratory analyses for keywords within the instrument family categories (Table 1 and Tables S6–S11, online only).

We conducted an additional set of analyses restricted to children/adolescents (individuals with a median age of record between the ages of 5 and 18 years old; Table S12, online only).

Results

Associations with musician status

For our primary analyses, we identified 9803 adult cases (58% males, mean age (SD) = 47.8 (17.2) years) as musicians, who we compared with 49,015 controls (60% males, mean age (SD) = 47.5 (17.4) years), defined by the absence of the above-listed musician keywords in their EHR, and matched for the median age of record, sex, the length of record, the number of visits, race, and ethnicity (Table 1).

Two hundred fifty-seven phenotypes were significantly associated with musician status ($P < 7.6 \times 10^{-6}$, accounting for multiple testing) (Figs. 2 and 3; for the full table, see Table S3, online only). Out of these, 242 diagnoses were more commonly observed among musicians and 15 diagnoses were more commonly observed among controls. Among the top diagnoses enriched in musicians were diseases of the larynx and vocal cords (OR = 2.32 (95% CI: 2.25–2.40)), voice disturbance (OR = 2.43 (95% CI: 2.34–2.51)), hearing loss (OR = 1.36 (95% CI: 1.32–1.39)), pain in joint (OR = 1.26 (95% CI: 1.23–1.28)), anxiety disorder (OR = 1.25 (95% CI: 1.22–1.28)), sleep disorders (1.23 (95% CI: 1.19–1.26)), and back pain (OR = 1.17 (95% CI: 1.15–1.20)). Chronic laryngitis (OR = 3.02 (95% CI: 2.80–3.25)) and voice disturbance (OR = 2.43 (95% CI: 2.34–2.51)) had the largest effect sizes. We summarized the top association within each medical diagnosis group in Table 2. Among the top phenotypes observed more frequently in controls were coronary atherosclerosis (OR = 0.91 (95% CI: 0.89–0.94)), respiratory failure/insufficiency/arrest (OR = 0.89 (95% CI: 0.86–0.93)), renal failure (OR = 0.93 (95% CI: 0.90–0.96)), and ischemic heart disease (OR = 0.92 (95% CI: 0.90–0.95)). (see Table 3 for a summary of the number of diseases within the phecode categories). The results remained virtually unchanged when we adjusted for the median BMI (Table S5, online only).

When we restricted the analyses to males, there were 135 diagnoses that were significantly associated with musician status ($P < 7.6 \times 10^{-6}$) (Fig. 3 and Table S4, online only). Among those diagnoses, 130 were more common among male musicians compared with male controls. These were similar to the whole sample, including voice disturbance (OR = 2.20 (95% CI: 2.15–2.25)), tinnitus (OR = 1.60 (95% CI: 1.54–1.65)), generalized anxiety disorder (OR = 1.38 (95% CI: 1.31–1.44)), mood disorders (OR = 1.23, (95% CI: 1.20–1.26)), and cervicalgia (OR = 1.38 (95% CI: 1.34–1.41)). There were also five diagnoses that were less common among male musicians compared with male controls, including ischemic heart disease (OR = 0.92 (95% CI: 0.89–0.95)), coronary atherosclerosis (OR = 0.91, (95% CI: 0.88–0.95)),

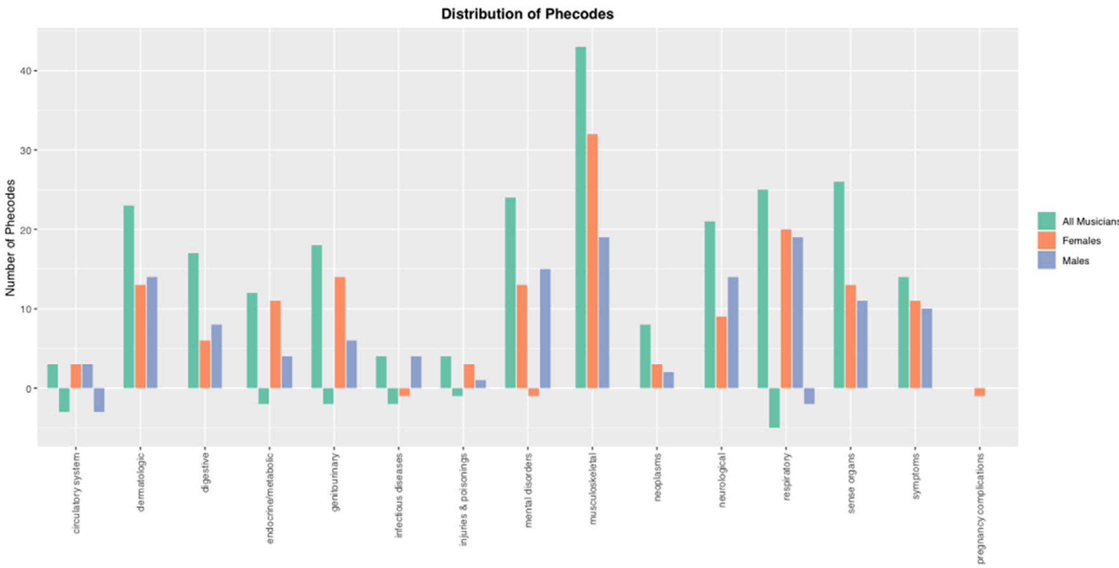

Figure 3. **Phecode categories significantly associated with musicians. The *x*-axis shows the phecode categories per group (i.e., all musicians, females, and males), while the *y*-axis shows the number of phecodes per the phecode category.**

and congestive heart failure/nonhypertensive (OR = 0.90 (95% CI: 0.86–0.94)).

Analyses in females identified 154 diagnoses that were significantly associated with musician status ($P < 7.6 \times 10^{-6}$) (Fig. 3 and Table S4, online only). Again, these included voice disturbance (OR = 2.71 (95% CI: 2.66–2.76)), tinnitus (OR = 1.53 (95% CI: 1.45–1.61)), throat pain (OR = 1.52 (95% CI: 1.40–1.63)), and cervicalgia (OR = 1.53 (95% CI: 1.49–1.56)). There were three diagnoses that were less common among female musicians, including tobacco use disorder (OR = 0.85 (95% CI: 0.79–0.91)), known or suspected fetal abnormality affecting management of mother (OR = 0.87, (95% CI: 0.82–0.93)), and septicaemia (OR = 0.83 (95% CI: 0.75–0.91)).

To examine whether the difference in the ORs between males and females was significantly different, we performed an interaction test (Sex * Musician/nonmusician; Table S4, online only). Voice disturbance, tinnitus, pain in joint, as well as a number of other diagnoses were significantly more common among female musicians. On the other hand, mental health disorders, including anxiety disorder, depression, bipolar disorder, alcohol-related disorders, and substance addiction and disorders, were significantly more common among male musicians. Thus, after accounting for the different baseline prevalence of these disorders between males and females, there remains a significant difference in the strength of association between male and female musicians.

String instrument players

We stratified to 3209 players of string instruments (75% males) versus 16,045 (76% males) controls (Table 1). One hundred forty-eight diagnoses were significantly more common among players of string instruments ($P < 7.6 \times 10^{-6}$) (Table S6 and Figs. S1 and S2, online only). Among the top associations positively associated with string instrument players were diseases of larynx and vocal cords (OR = 1.77 (95% CI: 1.66–1.88)), voice disturbance (OR = 1.88 (95% CI:1.76–2.01)), tinnitus (OR = 1.49 (95% CI: 1.37–1.62)), synovitis and tenosynovitis (OR = 1.68 (95% CI: 1.58–1.79)), stiffness of the joint (OR = 1.63 (95% CI: 1.52–1.73)), and fasciitis (OR = 1.49 (1.34–1.63)).

Percussionists

Eight hundred eighty-six players of percussion instruments (84% males) and 4430 controls (85% males) were identified and included in the analyses (Table 1). Nineteen diagnoses were significantly associated with players of percussion instruments ($P < 7.6 \times 10^{-6}$) (Table S7 and Figs. S1 and S3, online only). Tinnitus (OR = 1.63 (95% CI: 1.41–

Ann. N.Y. Acad. Sci. 1505 (2021) 156–168 © 2021 The Authors. *Annals of the New York Academy of Sciences* published by Wiley Periodicals LLC on behalf of New York Academy of Sciences

Table 2. Top specific diagnostic associations with musician status per the phecode

Group	Diagnosis	OR	*P* value
Respiratory	Voice disturbance	2.43	$<2.84 \times 10^{-191}$
Musculoskeletal	Pain in joint	1.26	1.09×10^{-125}
Symptoms	Cervicalgia	1.45	2.25×10^{-184}
Sense organs	Hearing loss	1.36	5.98×10^{-97}
Digestive	GERD	1.21	9.13×10^{-62}
Mental disorders	Anxiety disorder	1.25	7.67×10^{-71}
Neurological	Sleep disorders	1.23	1.55×10^{-47}
Endocrine/metabolic	Vitamin D deficiency	1.15	1.48×10^{-18}
Dermatologic	Disturbance of skin sensations	1.24	4.51×10^{-29}
Genitourinary	Menopausal and postmenopausal disorders	1.21	3.77×10^{-23}
Circulatory	Palpitations	1.18	1.34×10^{-27}
Neoplasms	Benign neoplasm of skin	1.24	4.18×10^{-27}
Infectious diseases	Viral warts and HPV	1.19	7.81×10^{-12}
Injuries and poisonings	Sprains and strains	1.14	7.93×10^{-15}

1.86)), generalized anxiety disorder (OR = 1.53 (95% CI: 1.30–1.75)), asthma (OR = 1.32 (95% CI: 1.19–1.45)), and cervicalgia (OR = 1.30 (95% CI: 1.18–1.42)) were among the top associations.

Keyboard players

Two-thousand one hundred six players of keyboards (35% males) and 10,530 controls (35% males) were included in the analyses (Table 1). Fifty-nine diagnoses were associated with players of keyboard instruments ($P < 7.6 \times 10^{-6}$) (Table S8 and Figs. S1 and S4, online only). Among these, 55 diagnoses were positively associated with keyboard players, including voice disturbance (OR = 1.56 (95% CI: 1.49–1.64)), synovitis and tenosynovitis (OR = 1.49 (95% CI: 1.42–1.57)), stiffness of the joint (OR = 1.52 (95% CI: 1.45–1.59)), and tinnitus (OR = 1.39 (95% CI: 1.29–1.49)). Four diagnoses were negatively associated with keyboard players, including coronary atherosclerosis (OR = 0.86 (95% CI: 0.81–0.92)), ischemic heart disease (OR = 0.88 (95% CI: 0.83–0.93), congestive heart failure; nonhypertensive (OR = 0.85, 95% CI: 0.79–0.92)), pleurisy; pleural effusion (OR = 0.82 (95% CI: 0.74–0.90)).

Brass instrument players

Three-hundred forty brass players (72% males) versus 1700 controls (74% males) were identified (Table 1). Allergic rhinitis was the only significant association (OR = 1.39, 95% CI: 1.25–1.52, $P = 1.22 \times 10^{-06}$) (Table S9, online only).

Woodwind instrument players

We included 482 (39% males) players of woodwinds versus 2410 (40% males) controls in the analyses (Table 1). There were eight significant associations ($P < 7.6 \times 10^{-6}$). Pain in joint was the strongest association (OR = 1.26, 95% CI: 1.19–1.36)), while myopia had the largest effect size (OR = 1.47, 95% CI: 1.32–1.62) (Table S10, online only).

Vocalists

Two-thousand three-hundred eighty-seven vocalists (43% males) and 11,935 controls (44% males) were included in the analyses (Table 1). Sixty-two diagnoses were associated with vocalists ($P < 7.6 \times 10^{-6}$) (Table S11 and Figs. S1 and S7, online only). As expected, among the top associations were diseases of the larynx and vocal cords (OR = 4.87 (95% CI: 4.56–5.18)), chronic laryngitis (OR = 6.64 (95% CI: 5.66–7.62)), and voice disturbance (OR = 5.13 (95% CI: 4.78–5.47)). Other strong associations were throat pain (OR = 2.28 (95% CI: 1.98–2.59)), hearing loss (OR = 1.28 (95% CI:1.20–1.36)), gastroesophageal reflux disease (OR = 1.57 (95% CI: 1.50–1.63)), cervicalgia (OR = 1.75 (95% CI: 1.67–1.83)), and sleep disorders (OR = 1.15 (95% CI: 1.08–1.22)).

To address the possibility that the string instrument and keyboard players suffer vocal-related problems because they may also sing regularly, we determined that 9.6% of string musicians and 6.8% of keyboard players were also vocalists. Then, to determine whether these individuals accounted for

Table 3. Summary of the number of diseases within phecode categories

Associations
Positive associations
• 3 disorders of the circulatory system (e.g., palpitations and nonspecific chest pain)
• 23 dermatologic disorders (e.g., disturbance of skin sensation and seborrheic keratosis)
• 17 digestive disorders (e.g., gastroesophageal reflux disease and irritable bowel syndrome)
• 12 endocrine/metabolic disorders (e.g., vitamin D deficiency and hypercholesterolemia)
• 18 genitourinary disorders (e.g., menopausal/postmenopausal disorders)
• 4 infectious diseases (e.g., HPV and dermatophytosis/dermatomycosis)
• 4 injuries and poisonings (e.g, sprains and strains, and fractures)
• 24 mental disorders (e.g., anxiety disorder, mood disorders, and depression)
• 43 musculoskeletal disorders (e.g., pain in joint, synovitis, and tenosynovitis)
• 8 neoplasms (e.g., benign neoplasm of skin)
• 21 neurological disorders (e.g., sleep disorder, abnormal movements, and insomnia)
• 25 respiratory (e.g., diseases of larynx and vocal cords, voice disturbance, and allergic rhinitis)
• 26 sense organs (i.e., hearing loss and tinnitus)
• 14 symptoms (e.g., cervicalgia, malaise, and fatigue)
Negative associations
• 3 disorders of the circulatory system (e.g., coronary atherosclerosis and ischemic heart disease)
• 2 endocrine/metabolic disorders (i.e., acidosis, acid–base balance disorder, and diabetes mellitus)
• 2 genitourinary disorders (i.e., renal and acute renal failure)
• 2 infectious diseases (i.e., bacterial infection NOS and septicemia)
• 1 injuries and poisonings (i.e., sepsis and SIRS)
• 5 respiratory (e.g., respiratory failure and pleurisy)

the vocal problems, we performed a sensitivity analysis in which we removed from the string musicians and keyboard players those who were also vocalists. The associations with voice disturbance (string instrument players: OR = 1.44 (95% CI = 1.36–1.52), $P = 4.6 \times 10^{-19}$; and keyboard players: OR = 1.58 (95% CI = 1.50–1.65, $P = 2.9 \times 10^{-31}$)) and other vocal cord-related phenotypes (e.g., diseases of the larynx and the vocal cords) remained highly significant (string instrument players: OR = 1.42 (95% CI = 1.34–1.49), $P = 9.9 \times 10^{-20}$; and keyboard players: OR = 1.54 (95% CI = 1.47–1.61), $P = 3.2 \times 10^{-31}$)), indicating that there are likely more individuals in the dataset who are vocalists but for whom this is not noted in their chart.

Musicians between the ages of 5 and 18

There were 4576 cases of musicians between the ages of 5 and 18 years (mean age (SD) = 12.7 (3.5) years; 48% males) and 22,880 controls (mean age (SD) = 13.1 (3.6) years; 47% males). One-hundred fourteen diagnoses were associated with musician status in this age group ($P < 7.6 \times 10^{-6}$) (Table S12 and Fig. S8, online only). Among the strongest associations were anxiety disorder (OR = 1.32 (95% CI: 1.27–1.37)), depression (OR = 1.26 (95% CI: 1.21–1.31)), eating disorder (OR = 1.48 (95% CI: 1.36–1.59)), and voice disturbance (OR = 1.70 (95% CI:1.53–1.87). The largest effect was observed for voice disturbance (OR = 1.70 (95% CI:1.53–1.87)), followed by anorexia nervosa (OR = 1.56 (95% CI: 1.37–1.76)). For differences in the diagnoses between children and adults, see Table S13 (online only).

Discussion

In a sample of 14,379 musician cases and 71,895 matched controls identified in an EHR database, we conducted the first and largest study to date to identify medical phenotypes associated with musician patients in an EHR context. We first created and validated a novel musician phenotype identification method for use in EHR, which showed a PPV of 93%. We then replicated previous associations of musician status with medical problems, including musculoskeletal problems,[5] skin disorders,[6] respiratory and hearing problems,[7,2] as well as mental health problems,[10,29] and also detected novel associations. Furthermore, we identified protective effects for a number of diagnoses, including coronary atherosclerosis and renal failure. These findings are in line with a study indicating lower blood pressure and heart rate in musicians, compared with controls,[30] as well as studies suggesting that active music engagement has similar training effects to physical exercise,[30,31] and that music training is associated with neurological benefits.[21]

When we stratified our analyses by instrument family, results of health problems aligned with the type of instrument. There was substantial overlap in diagnoses associated with different instrument families as well as distinct patterns of effects analogous to the physical demands of each instrument. For example, for vocalists, the strongest associations were diseases of the larynx, and vocal cords, voice disturbance, and chronic laryngitis. Players of percussion instruments demonstrated higher rates of hearing loss, while players of string instruments were more commonly treated for pain in joint and cervicalgia as well as voice disturbance. Keyboard players experienced higher rates of pain and stiffness of the joint. These findings provide further face validity for the method of musician identification in the EHR and increase confidence in the novel associations presented.

When it comes to protective effects related to the family of instruments, these were restricted to keyboard players and, as in the total sample of musicians, were related to less risk for cardiovascular diseases. Although statistical power could be a factor why we did not see such effects for brass, woodwind, and percussion instrument players, this does not seem to be the case for players of string instruments and vocalists, as these samples were larger than the keyboard players. It is possible that playing keyboards has a greater cardiovascular benefit than playing string instruments or singing. The effect may be confounded by the music genre, years of training, or performance settings. Further studies are needed to better understand the underlying physiology at play and to replicate our findings.

We also found strong associations of musician status with a number of mental health disorders, some of which were already present in childhood and adolescence, including anxiety disorders, depression, posttraumatic stress disorder, and bipolar disorder, suggesting that musicians may benefit from mental health support integrated into musical training. The exact nature of the association between musical activities and mental health problems is unclear. A recent twin modeling study found that this association is more likely explained by shared genetic or environmental factors that affect both the risk for mental health problems and musical achievement.[32] Evidence for shared genetic or environmental susceptibility also comes from a study that found that higher polygenic scores for schizophrenia and bipolar disorder were associated with artistic society membership or a creative profession.[33] However, this does not rule out the potential for engagement in music as a therapeutic for existing mental health problems, which could also explain our findings.

A previous study on 377 musicians reported that the chief symptoms of musicians were mental health related—performance-related anxiety, social anxiety, and depression—and were more common in female musicians.[3] We found that although the effect sizes of depression and anxiety-related disorders are slightly higher in males, such problems were strongly associated with both male and female musicians.

Our study included a total of 86,274 individuals. This unprecedented sample size provided us with the statistical power to be able to detect the prevalence of 257 diagnoses that were more common among musicians than controls. Several of those diagnostic associations have not been previously described in the literature, including circulatory, genitourinary, and endocrine/metabolic disorders. Though speculative, a subset of these disorders may be associated with environmental risk factors associated with being a musician.

In addition to mental health disorders, our study identified a wide range of other disorders that healthcare professionals should be aware of to provide treatment personalized to the needs of musicians. Furthermore, our study demonstrates how information on a persons' occupational and vocational history can provide useful insights in terms of preventing and anticipating medical problems that may be related to a specific occupation.[34] Therefore, it is possible that the effect sizes for certain disorders that are directly related to a person's ability to perform their music (e.g., voice disturbance) are larger than the true estimate, given that individuals may not seek treatment for issues that are less likely to affect their professional life. Future studies in the healthcare context could use

EHRs to identify risks associated with other types of occupation. Finally, we found protective effects of being a musician, including a lower risk for coronary atherosclerosis and renal failure, providing further evidence for potential cardiovascular benefits associated with the increased physiological and mental demands associated with music training.

Despite the enormous power that research in the EHR provides, there are certain limitations of the current approach. We were not able to determine from the records whether an individual is an amateur versus a professional musician, how many years of training they had, whether they are part of an ensemble or a solo musician, or the music genre. We were also not able to know if the types of disorders and symptoms that were more commonly observed in musicians were related to the nature of their music activity. For instance, we do not know if there are differences in the way people who play violin in a classic orchestra practice it differently than people who play violin (fiddle) in a bluegrass band. Although we sometimes had information on the type of instrument, this was not always the case, as we would often encounter charts reporting "musician" as the only relevant keyword. Also, future studies can examine whether there are differences in health problems between single- and multi-instrumentalists. Another limitation related to the EHR is that the health records are noisy, taking into account that they were evaluated by different health providers at different times. Moreover, we were not able to obtain a systematic history of musical involvement. There is also the possibility that a physician/nurse practitioner is more likely to identify a patient as a musician if their chief complaint during a clinical encounter is related to their music. The impact of this in our results could be a differential loss of power across diagnoses, which would, in turn, make it difficult to compare the effect sizes between different phenotypes. However, it is noteworthy that in our longitudinal EHR, patients accumulate many diagnoses over time. Thus, while any given visit may be related to musicianship, it is unlikely that all visits are related to musicianship. This allows us to investigate a range of phenotypes that are not necessarily attributed to musician status. VUMC has specialty clinics, including a voice clinic, that attracts individuals from across the country, and therefore, such specialty clinics may enrich different disorders and symptoms. Finally, future studies could investigate more fine-tuned hypothesis-driven specific phenotyping (i.e., enrolling musicians in the comprehensive questionnaire or clinician report to delve into particular associations suggested by the PheWAS).

Conclusions

We conducted the first PheWAS of musicians using an EHR framework in over 80,000 individuals and found both the risk and protective associations with many medical disorders. These included medical complaints involving the musculoskeletal, respiratory, endocrine, and metabolic systems, and mental health problems. On the other hand, we also identified a number of protective effects by observing diagnoses, such as cardiovascular disease and respiratory and renal failure, which were less common in musicians than in controls, in line with the literature indicating that active musical engagement has similar health benefits to athletic engagement. Although musical training usually focuses on performance and musical achievement, it is also important to address the physical and psychological health needs of musicians.[35] Indeed, our study highlights the need for management, prevention, and health education of musicians and the healthcare providers treating them. Finally, this study serves as a proof of principle to demonstrate that EHR studies, and PheWAS in particular, can be effectively used to identify medical disorders associated with specific occupations.

Acknowledgments

This project was supported by funding from the National Institutes of Health, the NIH Common Fund through the Office of the NIH Director under Award Number DP2HD098859. L.K.D. was supported by grants from the National Institutes of Health, including R01MH118223, R01DC16977, and R56MH120736. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. We would also like to thank the Nashville Musicians Association and especially Kathy Osborne for providing us with the list of the most popular musical instruments.

Synthetic Derivative

The Synthetic Derivative resource was supported by the National Center for Research Resources, Grant

UL1 RR024975-01, and is now at the National Center for Advancing Translational Sciences, Grant 2 UL1 TR000445-06. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Author contributions

M.N., L.K.D., and R.L.G. devised the study concept and design. M.N., G.L., and L.K.D. were responsible for acquisition of data and data analyses. M.N., L.K.D., R.L.G., and M.D.L. interpreted the data. All authors critically revised the manuscript for important intellectual content.

Supporting information

Additional supporting information may be found in the online version of this article.

Table S1. Counts of types of instruments played by professional musicians from Nashville musicians association as retrieved on August 20, 2019.

Table S2. List of keywords and regular expressions.

Table S3. PheWAS results of musicians.

Table S4. PheWAS results of musicians stratified by gender and results from musicians by gender interaction.

Table S5. PheWAS results of musicians further adjusting for the median BMI.

Table S6. PheWAS results of string instruments.

Table S7. PheWAS results of percussion instruments.

Table S8. PheWAS results of keyboards instruments.

Table S9. PheWAS results of brass instruments.

Table S10. PheWAS results of woodwinds.

Table S11. PheWAS results of vocalists.

Table S12. PheWAS results of musicians between the ages of 5 and 18 years old.

Table S13. Differences in the PheWAS results between children and adults.

Figure S1. Bar plots of number of diagnoses/conditions per phecode category.

Figure S2. PheWAS plot of conditions associated with string instruments players.

Figure S3. PheWAS plot of conditions associated with percussionists.

Figure S4. PheWAS plot of conditions associated with keyboard players.

Figure S5. PheWAS plot of conditions associated with brass players.

Figure S6. PheWAS plot of conditions associated with woodwind players.

Figure S7. PheWAS plot of vocalists.

Figure S8. PheWAS plot of child musicians, ages 5–18.

Competing interests

The authors declare no competing interests.

References

1. Wills, G.I. & C.L. Cooper. 1987. Stress and professional popular musicians. *Stress Med.* **3:** 267–275.
2. Žuškin, E., E.N. Schachter, I. Kolčić, *et al.* 2005. Health problems in musicians—a review. *Acta Dermatovenerol. Croat.* **13:** 247–251.
3. Kenny, D., T. Driscoll & B. Ackermann. 2014. Psychological well-being in professional orchestral musicians in Australia: a descriptive population study. *Psychol. Music* **42:** 210–232.
4. Gomez-Rodriguez, R., B. Diaz-Pulido, C. Gutierrez-Ortega, *et al.* 2020. Prevalence, disability and associated factors of playing-related musculoskeletal pain among musicians: a population-based cross-sectional descriptive study. *Int. J. Environ. Res. Public Health* **17:** 3991.
5. Blanco-Piñeiro, P., M.P. Díaz-Pereira & A. Martínez. 2017. Musicians, postural quality and musculoskeletal health: a literature's review. *J. Bodywork Move. Therap.* **21:** 157–172.
6. Patruno, C., M. Napolitano, S. La Bella, *et al.* 2016. Instrument-related skin disorders in musicians. *Dermatitis* **27:** 26–29.
7. Antoniadou, M., V. Michailidis, E. Perantoni, *et al.* 2011. Respiratory symptoms and risk for obstructive sleep apnea in professional musicians. *Eur. Respir. Soc*. **38:** 2279.
8. van Kemenade, J.F., M.J. van Son & N.C. van Heesch. 1995. Performance anxiety among professional musicians in symphonic orchestras: a self-report study. *Psychol. Rep.* **77:** 555–562.
9. Vaag, J., J.H. Bjørngaard & O. Bjerkeset. 2016. Symptoms of anxiety and depression among Norwegian musicians compared to the general workforce. *Psychol. Music* **44:** 234–248.
10. Van den Eynde, J., A. Fisher & C. Sonn. 2016. Working in the Australian Entertainment Industry. Entertainment Assist, Victoria University.
11. Vaag, J., I. Saksvik-Lehouillier, J.H. Bjørngaard & O. Bjerkeset. 2016. Sleep difficulties and insomnia symptoms in Norwegian musicians compared to the general population and workforce. *Behav. Sleep Med.* **14:** 325–342.
12. Forsyth, A.J.M., J.C. Lennox & C. Emslie. 2016. "That's cool, you're a musician and you drink": exploring entertainers'

accounts of their unique workplace relationship with alcohol. *Int. J. Drug Policy* **36:** 85–94.

13. Bellis, M.A., T. Hennell, C. Lushey, *et al.* 2007. Elvis to Eminem: quantifying the price of fame through early mortality of European and North American rock and pop stars. *J. Epidemiol. Commun. Health* **61:** 896–901.
14. Prior, B., E. Barra & S. Kramer. 2019. Women in the U.S. Music Industry: Obstacles and Opportunitis. https://college.berklee.edu/sites/default/files/d7/bcm/Women%20in%20the%20U.S.%20Music%20Industry%20Report.pdf.
15. Wang, Y. & E.-Á. Horvát. 2019. Gender differences in the global music industry: evidence from Musicbrainz and The Echo Nest. In Proceedings of the International AAAI Conference on Web and Social Media, pp. 517–526.
16. Fjellman-Wiklund, A., C. Brulin & G. Sundelin. 2003. Physical and psychosocial work-related risk factors associated with neck-shoulder discomfort in male and female music teachers. *Med. Probl. Perform. Art.* **18:** 33–41.
17. Savage, P.E., P. Loui, B. Tarr, *et al.* 2020. Music as a coevolved system for social bonding. *Behav. Brain Sci.* 1–42. https://doi.org/10.1017/S0140525X20000333
18. Bugos, J.A., W.M. Perlstein, C.S. McCrae, *et al.* 2007. Individualized piano instruction enhances executive functioning and working memory in older adults. *Aging Ment. Health* **11:** 464–471.
19. Diaz Abrahan, V., F. Shifres & N. Justel. 2019. Cognitive benefits from a musical activity in older adults. *Front. Psychol.* **10:** 652.
20. Terry, P.C., C.I. Karageorghis, M.L. Curran, *et al.* 2020. Effects of music in exercise and sport: a meta-analytic review. *Psychol. Bull.* **146:** 91–117.
21. Yoo, J. & G.M. Bidelman. 2019. Linguistic, perceptual, and cognitive factors underlying musicians' benefits in noise-degraded speech perception. *Hear. Res.* **377:** 189–195.
22. Cheever, T., A. Taylor, R. Finkelstein, *et al.* 2018. NIH/Kennedy Center Workshop on Music and the Brain: finding harmony. *Neuron* **97:** 1214–1218.
23. James, C.E., S. Zuber, E. Dupuis-Lozeron, *et al.* 2020. Formal string instrument training in a class setting enhances cognitive and sensorimotor development of primary school children. *Front. Neurosci.* **14:** 567.
24. Iñesta, M.C.J. 2006. *Demanda Fisiológica En Músicos Profesionales*. Universidad de Oviedo.
25. Denny, J.C., L. Bastarache, M.D. Ritchie, *et al.* 2013. Systematic comparison of phenome-wide association study of electronic medical record data and genome-wide association study data. *Nat. Biotechnol.* **31:** 1102–1110.
26. Roden, D.M., J.M. Pulley, M.A. Basford, *et al.* 2008. Development of a large-scale de-identified DNA biobank to enable personalized medicine. *Clin. Pharmacol. Ther.* **84:** 362–369.
27. Denny, J.C., M.D. Ritchie, M.A. Basford, *et al.* 2010. PheWAS: demonstrating the feasibility of a phenome-wide scan to discover gene–disease associations. *Bioinformatics* **26:** 1205–1210.
28. Anticevic, A., J.X. Van Snellenberg, R.E. Cohen, *et al.* 2012. Amygdala recruitment in schizophrenia in response to aversive emotional material: a meta-analysis of neuroimaging studies. *Schizophr. Bull.* **38:** 608–621.
29. Bonde, L.O., K. Juel & O. Ekholm. 2018. Associations between music and health-related outcomes in adult non-musicians, amateur musicians and professional musicians—results from a nationwide Danish study. *Nordic J. Music Ther.* **27:** 262–282.
30. Burggraaf, J.L., T.W. Elffers, F.M. Segeth, *et al.* 2013. Neurocardiological differences between musicians and control subjects. *Neth. Heart J.* **21:** 183–188.
31. Vellers, H.L., C. Irwin & J.T. Lightfoot. 2015. Heart rate response of professional musicians when playing music. *Med. Probl. Perform. Art.* **30:** 100–105.
32. Wesseldijk, L.W., F. Ullén & M.A. Mosing. 2019. The effects of playing music on mental health outcomes. *Sci. Rep.* **9:** 1–9.
33. Power, R.A., S. Steinberg, G. Bjornsdottir, *et al.* 2015. Polygenic risk scores for schizophrenia and bipolar disorder predict creativity. *Nat. Neurosci.* **18:** 953.
34. Couth, S., N. Mazlan, D.R. Moore, *et al.* 2019. Hearing difficulties and tinnitus in construction, agricultural, music, and finance industries: contributions of demographic, health, and lifestyle factors. *Trends Hear.* **23**: 2331216519885571.
35. Chong, J.P. 2018. Musicians' health problems: a psychophysiological approach. In *Performing Arts Medicine*. L.E. Elson, Ed.: 35–44. Elsevier.