Twenty-year incidence rates of cardiovascular disease in Greece: A geospatial analysis in the Attica study context, 2002-2022

Antigoni Faka[1], Evangelia Damigou[2], Christina Chrysohoou[3], Fotios Barkas[4], Elpiniki Vlachopoulou[2], Dimitris Dalmyras[2], Christina Vafia[2], Evangelinos Michelis[3], Asimina Loukina[3], Georgios Mentzantonakis[3], Petros S. Adamidis[4], Georgia Anastasiou[4], Amalia D. Koutsogianni[4], Christos Chalkias[1], Christos Pitsavos[3], Evangelos Liberopoulos[5], Costas Tsioufis[3], Petros P. Sfikakis[5], Demosthenes Panagiotakos[2]

[1]Department of Geography, School of Environmental Sciences and Economics, Harokopio University, Athens, Greece, [2]Department of Nutrition and Dietetics, School of Health Sciences and Education, Harokopio University, Athens, Greece, [3]First Cardiology Clinic, Medical School, National and Kapodistrian University of Athens, Hippokration Hospital, Athens, Greece, [4]Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece, [5]First Department of Propaedeutic Internal Medicine, Medical School, Laiko General Hospital, National and Kapodistrian University of Athens, Athens, Greece

ABSTRACT

Aim: The aim of this study was to explore the geographical disparities in CVD incidence across the Attica region, over a 20-year period.

Material and Methods: The 10-year and the 20-year CVD incidence data were provided by the ATTICA study, which was conducted during 2002-2022 in 3042 individuals living in Attica region. After excluding those lacking complete locality information and those lost in the 10-year and the 20-year follow-up, data for 1935 and 1902 individuals respectively, were used for the current analysis. CVD incidence rates at municipality level were mapped and hot spot analysis was implemented to recognize statistically significant spatial clusters in Attica region.

Results: Mapping CVD incidence rates revealed a notable rise during the 20 years in most municipalities. The rise in female-specific CVD incidence appeared primarily in suburban areas, while a significant rise in male-specific CVD incidence was noticed in urban areas. Statistically significant spatial clusters of high values were indicated in the most urbanized municipalities of the study area, whereas clusters of low values were noticed in the more distant rural municipalities, which maintained lower CVD incidence rates during the monitoring period.

Conclusions: A spatial heterogeneity of the sex-specific 20-year CVD incidence rate was observed in the Attica region of Greece.

KEY WORDS: *Geospatial analysis, cardiovascular disease, incidence, risk, Attica, Greece*

Corresponding author:

Demosthenes Panagiotakos
Harokopio University of Athens
70 El. Venizelou Ave., Kallithea, 176 76, Athens, Greece
Tel.: +30 210 9549332, E-mail: dbpanag@hua.gr

INTRODUCTION

Based on the most recent reports from the World Health Organization (WHO), cardiovascular diseases (CVD) are the number one cause of morbidity and mortality globally, accounting for approximately 30% of all deaths.[1] However, the exact cause of CVD is not completely understood as a considerable proportion of incident cases were without any risk factors.[2] It has also been reported that the prevalence of CVD varies by geographical region, as well as gender, race and living environmental conditions.

In Greece, CVDs remain the primary cause of death and disability, despite the progressions that have been made the past decades in primary, but more consistently in secondary prevention settings.[3] Although several epidemiological studies have assessed prevalence of CVD and related risk factors, in Greece, limited studies have focused on the geographical distribution of prevalent CVD, and no study has associated incidence of CVD with region of residence. Thus, the purpose of this study was to evaluate the geographical distribution of CVD incidence, in the Attica region, through a period of 20 years of the general population monitoring, from 2002 to 2022.

MATERIAL AND METHODS

Design

Data for the present study were obtained from a health and nutrition prospective cohort study, the ATTICA study. The study was initiated in 2001–2002, based on a representative (census 2001), population-based sampling scheme from all cities of the Attica (or Attiki) region, in Greece (including the metropolitan city of Athens),[4] and continued for 20 years with three subsequent follow-up examinations, in 2006, 2011–2012, and 2022, respectively.[5-7]

Sample

A representative sample of 3042 apparently healthy volunteers (free of CVD and other chronic diseases), in the 58 municipalities of Attica region, agreed to participate (75% participation rate). Of the enrolled participants, 1514 (49.8%) were men [mean age = 46 (SD = 13) years old] and 1528 (50.2%) were women [mean age = 45 (SD = 14) years old]. Of the 3042 initially enrolled participants, 2020 were found during the 10-year follow-up (66% participation rate), and 1988 participants were found in the 20-year follow-up (65% participation rate). No significant differences were observed in basic demographic characteristics between those who were lost to follow up and the rest.[7]

Bioethics

The study was carried out in accordance with the Dec-laration of Helsinki (1989) of the World Medical Association and was approved by the Institutional Ethics committee of Athens Medical School (#017/1.5.2001). All participants were informed about the study aims and provided written consent to participate in the study.

Cardiovascular outcomes assessment

The development of a first, fatal or non-fatal CVD event during the follow-up examinations was defined as the emergence of myocardial infarction, angina pectoris, or other identified forms of ischemia, heart failure of various types, chronic arrhythmias, or the onset of a stroke, according to the 10th WHO International Coding of Disease classification (ICD-10).

The sample used for the current analysis consisted of 1935 participants from the 10-year follow-up and 1902 from the 20-year follow-up examination, with complete data on locality and CVD event development. For this study, the 10-year and 20-year CVD incidence at the municipality level was used, as the ATTICA study's sample was representative of each municipality population.

Spatial Analysis

Geographic Information Systems (GIS) technology was used to map CVD incidence across Attica municipalities and identify hotspots of high-risk areas. A spatial database was created, including the epidemiological data and the spatial layers of the 58 administrative units (municipalities). The geocoding of participants' characteristics from the ATTICA study relied on their residential addresses, assigning each observation to the respective spatial unit. The data were aggregated by municipality, and the 10-year and 20-year CVD incidence (%) for the total population, as well as for men and women, were calculated.

Hot-Spot-Analysis was conducted using Getis-Ord Gi* statistic to identify significant spatial clusters of both high and low values. The standardized Gi* is essentially a z-value of each spatial unit in a dataset, factoring in the unit's value, neighboring units' values, and the overall distribution of values across the study area. The z-score is linked to statistical significance at confidence levels of 99%, 95%, and 90%, indicating whether a spatial unit has notably high or low values compared to its neighboring units and whether they cluster spatially.

The spatial relationship conceptualization and the distance method should be set in Hot Spot Analysis. The spatial relationship conceptualization was based on the fixed distance band, where each spatial unit is analyzed in relation to its neighboring spatial units by setting a critical distance. Spatial units inside the specified distance exert influence on computations for the target spatial unit,

whereas units outside the critical distance have no influence on the target unit's computations. In this analysis, the optimal fixed distance band, based on peak clustering, was calculated and set for each dataset.

Spatial analysis resulted in a set of thematic maps illustrating the spatial distribution of CVD incidence (%), and the areas with statistically significant high (hot spots) or low values (cold spots). The incidence values were classified using common class intervals for both the 10-year and 20-year data, to ensure comparability of the results. The classification was based on the statistical mean of the total population CVD incidence in the Attica region. In the produced maps, five classes were specified based on the region's mean value, creating a central class, and the respective statistical means of the values below and above the region's average, defining the two lower and the two upper classes respectively. Details about the methods and inference made may be found elsewhere.[8-10]

Spatial analysis and mapping were performed using ArcGIS version 10.2 (ESRI Inc., Redlands, California, USA).

RESULTS

Mapping CVD incidence in the Attica region indicated higher 20-year CVD incidence rates compared to the 10-year CVD incidence across the majority of the municipalities (Figures 1a, 1d). The rise of the CVD incidence between the two periods is noticed mainly in the urban municipalities within the metropolitan area of Athens, whereas the rural municipalities maintained lower rates. Municipality level rates on male-specific CVD incidence were higher than female-specific in both follow-up studies (Figures 1b, 1c, 1e, 1f), though the female-specific CVD incidence was increased in many municipalities as well (Figure 1f).

Hot-spot analysis revealed significant hot and cold spots only for the total population and the male-specific 20-year CVD incidence (Figures 2a, 2b). All hot spots are located in the central urban metropolitan area of Athens, while the cold spots both in total population and male-specific 20-year CVD incidence are noticed in the more distant rural municipalities.

DISCUSSION

The aim of this brief report was to present the spatial distribution of CVD incidence in the Attica region, in Greece, based on a very long-term follow-up period. It was observed that a significant increase in 10-year CVD incidence was limited to a few municipalities. However, in the 20-year follow-up, a notable rise was observed across most municipalities, primarily concentrated in urban areas. The increased rates in urban areas are mainly attributed to male-specific CVD incidence, revealing statistically significant spatial clusters of high values.
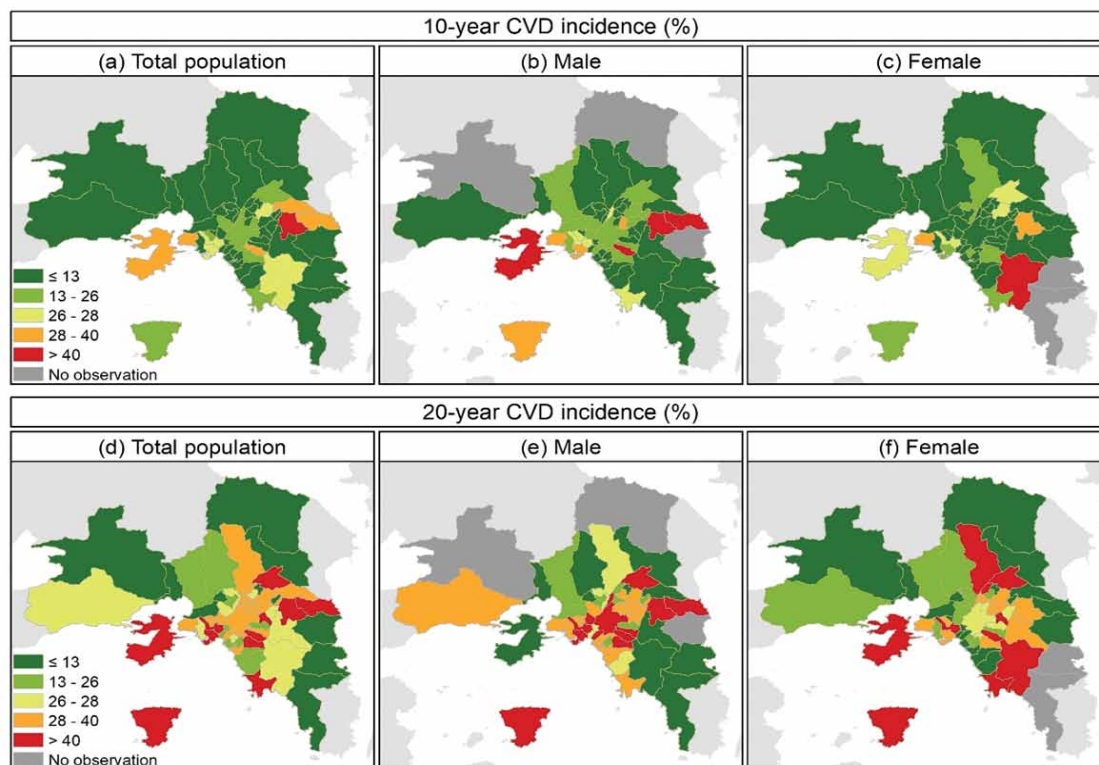

FIGURE 1. Spatial variability of the sex-specific 10-year and 20-year incidence of CVD across Attica municipalities in 2012 and 2022.
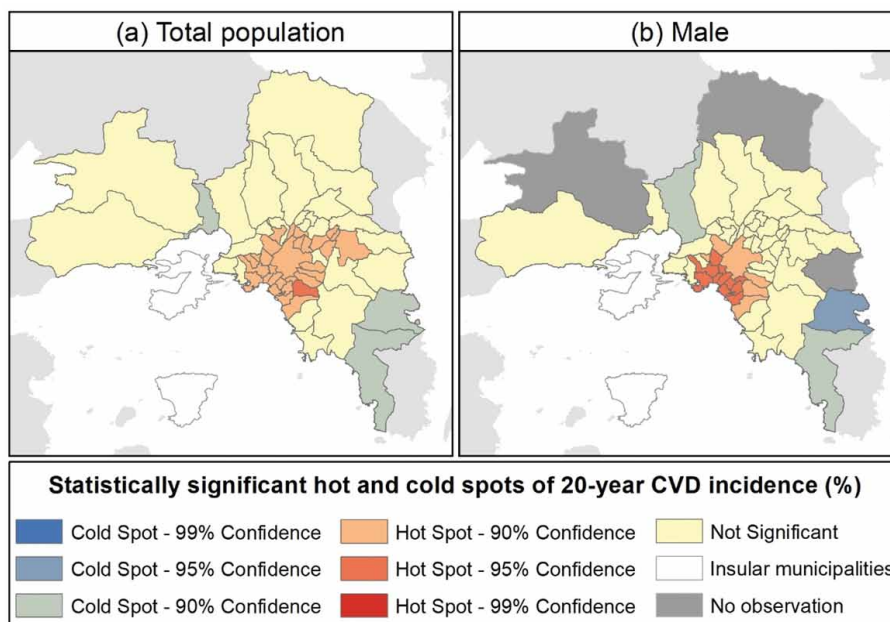
FIGURE 2. Hot and cold spots of the 20-year CVD incidence, 2022.

Cardiovascular disease epidemiology in Greece has its origins in the Seven Countries Study, where Ancel Keys and his Greek colleagues, Anastasios Dontas and Chris Aravanis, enrolled in the late 1950s about 1,300 men aged 40-59 years old from Crete and Corfu villages.[11] A key finding of the Seven Countries Study was that the Greek cohorts showed the lowest CVD incidence rates among all 16 cohorts of the 7 participating studies at 10 and 25 years of follow-up. Almost three decades after, in mid 1980s, Moulopoulos et al., evaluated risk factors for CVD in a random sample of 4,097 Athenian men and women. The main conclusion of the Athens Study was that the prevalence rates of CVD risk factors were the same or greater than those in industrialized countries.[12] The Attica Study was conducted in the beginning of 2000s, to evaluate the prevalence of CVD risk factors and related cardio-metabolic disorders, like obesity, diabetes, dyslipidemias and hypertension, as well as to assess the incidence of CVD in the long-term. The 5-year follow-up of the study revealed that 8.5% (11.0% men and 6.1% women) of the participants developed a CVD event during this period, while this rate was increased to 15.7% (19.7% men and 11.7% women) within 10 years, and to 36.1% (40.2% men and 32.1% women) within 20 years. Alongside the increase in CVD incidence rates over the years, a decrease in the man-to-woman ratio was observed, decreasing from 1.8 in the first 5 years to 1.6 within 10 years, and further down to 1.2 during 20 years.[5-7] It should also be noted that, during the 20-year follow-up, differences in the man-to-woman CVD incidence ratio were observed by age-group.[7]

In the present study a geospatial analysis was performed based on the 20-year follow-up data, highlighting the varying levels of CVD incidence rise between urban and rural areas, and the spatial heterogeneity between men and women CVD incidence rates. Future directions and analyses may reveal associations between CVD incidence and various environmental factors, like green areas coverage, proximity to parks, availability of sports facilities and other recreational areas that promote physical activity. Other studies from countries in Europe, Asia, Americas have shown there is an association between residential greenness and CVD outcomes, as living in greener neighborhoods and near parks encourage physical activity that exerts beneficial effects on cardiovascular health.[13-16]

Limitations

The aggregation of CVD outcomes data at the municipality level assumed a uniform distribution. However, it has to be acknowledged that the ATTICA study sample is representative of the population living in the Attica region. Furthermore, the variability in CVD incidence rates among neighborhoods within municipalities may lead to challenges related to the modifiable areal unit problem.

CONCLUSIONS

This study is the first study investigating the geographical variability of the sex-specific 20-year CVD incidence rate, demonstrating significant variations among Attica region's municipalities. This spatial heterogeneity may reflect differences in the environmental features of residential areas,

ΠΕΡΙΛΗΨΗ

Εικοσαετής επίπτωση καρδιαγγειακών συμβαμάτων στην Ελλάδα: Μια γεωχωρική ανάλυση στο πλαίσιο της μελέτης ΑΤΤΙΚΗ (2002-2022)

Αντιγόνη Φάκα[1], Ευαγγελία Δαμίγου[2], Χριστίνα Χρυσοχόου[3], Φώτιος Μπάρκας[4], Ελπινίκη Βλαχοπούλου[2], Δημήτρης Δαλμύρας[2], Χριστίνα Βαφία[2], Ευαγγελινός Μιχελής[3], Ασημίνα Λουκίνα[3], Γεώργιος Μεντζαντωνάκης[3], Πέτρος Σ. Αδαμίδης[4], Γεωργία Αναστασίου[4], Αμαλία Δ. Κουτσογιάννη[4], Χρίστος Χαλκιάς[1], Χρήστος Πίτσαβος[3], Ευάγγελος Λυμπερόπουλος[5], Κώστας Τσιούφης[3], Πέτρος Π. Σφηκάκης[5], Δημοσθένης Παναγιωτάκος[2]

[1]Τμήμα Γεωγραφίας, Σχολή Περιβάλλοντος, Γεωγραφίας & Εφαρμοσμένων Οικονομικών, Χαροκόπειο Πανεπιστήμιο, Αθήνα, Ελλάδα, [2]Τμήμα Επιστήμης Διαιτολογίας-Διατροφής, Σχολή Επιστημών Υγείας και Αγωγής, Χαροκόπειο Πανεπιστήμιο, Αθήνα, Ελλάδα, [3]Α' Καρδιολογική Κλινική, Ιατρική Σχολή, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, Ιπποκράτειο Νοσοκομείο, Αθήνα, Ελλάδα, [4]Τμήμα Εσωτερικής Παθολογίας, Ιατρική Σχολή, Πανεπιστήμιο Ιωαννίνων, Ιωάννινα, [5]Α' Τμήμα Προπαιδευτικής Παθολογίας, Ιατρική Σχολή, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, Γενικό Νοσοκομείο Λαϊκό, Αθήνα, Ελλάδα

Σκοπός: Σκοπός της παρούσας μελέτης ήταν να διερευνήσει τις χωρικές διαφοροποιήσεις στη συχνότητα εμφάνισης καρδιαγγειακών νοσημάτων στην περιοχή της Αττικής, σε μια περίοδο 20 ετών.

Υλικό και Μέθοδοι: Τα δεδομένα της επίπτωσης της καρδιαγγειακής νόσου 10 και 20 ετών προήλθαν από τη μελέτη ΑΤΤΙΚΗ, η οποία διεξήχθη την περίοδο 2002-2022 σε 3042 άτομα που κατοικούσαν στην περιοχή της Αττικής. Μετά τον αποκλεισμό εκείνων που δεν είχαν πλήρεις πληροφορίες για την τοποθεσία και εκείνων που χάθηκαν στη 10ετή και την 20ετή παρακολούθηση, για την τρέχουσα ανάλυση χρησιμοποιήθηκαν δεδομένα για 1935 και 1902 άτομα, αντίστοιχα. Τα ποσοστά εμφάνισης καρδιαγγειακών νοσημάτων σε επίπεδο δήμου χαρτογραφήθηκαν και εφαρμόστηκε ανάλυση hot spot για την αναγνώριση στατιστικά σημαντικών χωρικών συστάδων στην περιοχή της Αττικής.

Αποτελέσματα: Η χαρτογράφηση των ποσοστών εμφάνισης καρδιαγγειακών παθήσεων αποκάλυψε μια αξιοσημείωτη αύξηση κατά τη διάρκεια της 20ετίας στους περισσότερους δήμους. Η αύξηση της συχνότητας εμφάνισης καρδιαγγειακής νόσου ειδικά για γυναίκες εμφανίστηκε κυρίως σε προαστιακές περιοχές, ενώ σημαντική αύξηση στη συχνότητα εμφάνισης καρδιαγγειακής νόσου για άνδρες παρατηρήθηκε στις αστικές περιοχές. Στατιστικά σημαντικές χωρικές συστάδες υψηλών τιμών εντοπίστηκαν στους πιο αστικοποιημένους δήμους της περιοχής της Αττικής, ενώ συστάδες χαμηλών τιμών παρατηρήθηκαν στους πιο απομακρυσμένους αγροτικούς δήμους, οι οποίοι διατήρησαν χαμηλότερα ποσοστά εμφάνισης καρδιαγγειακής νόσου κατά την περίοδο παρακολούθησης.

Συμπεράσματα: Παρατηρήθηκε χωρική ετερογένεια της 20ετούς επίπτωσης καρδιαγγειακής νόσου που σχετίζεται με το φύλο στην περιοχή της Αττικής.

ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ: *Γεωχωρική ανάλυση, καρδιαγγειακά νοσήματα, επίπτωση, κίνδυνος, Αττική, Ελλάδα*

REFERENCES

1. Timmis A, Vardas P, Townsend N, Torbica A, Katus H, De Smedt D, et al. European Society of Cardiology: Cardiovascular disease statistics 2021. Eur Heart J. 2022 Jan;43(8):716-99.

2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990-2019: Update From the GBD 2019 Study. J Am Coll Cardiol. 2020 Dec;76(25):2982-3021.

3. Michas G, Karvelas G, Trikas A. Cardiovascular disease in Greece; The latest evidence on risk factors. Hellenic J Cardiol. 2019 Sep-Oct;60(5):271-5.

4. Pitsavos C, Panagiotakos DB, Chrysohoou C, Stefanadis C. Epidemiology of cardiovascular risk factors in Greece: Aims, design and baseline characteristics of the ATTICA study. BMC Public Health 2003 Oct;3:32.

5. Panagiotakos DB, Pitsavos C, Chrysohoou C, Skoumas I, Stefanadis C, & ATTICA Study group. Five-year incidence of cardiovascular disease and its predictors in Greece: The ATTICA study. Vasc Med. 2008;13(2):113–21.

6. Panagiotakos DB, Georgousopoulou EN, Pitsavos C, Chrysohoou C, Metaxa V, Georgiopoulos GA, et al. Ten-year (2002-2012) cardiovascular disease incidence and all-cause mortality, in urban Greek population: The ATTICA study. Int J Cardiol. 2015 Feb;180:178-84.

7. Damigou E, Kouvari M, Chrysohoou C, Barkas F, Kravvariti E, Pitsavos C, et al. Lifestyle Trajectories Are Associated with Incidence of Cardiovascular Disease: Highlights from the ATTICA Epidemiological Cohort Study (2002-2022). Life (Basel). 2023 May;13(5):1142.

8. Getis A, Ord JK. The analysis of spatial association by use of distance statistics. Geogr Anal. 1992;24(3):189–206.

9. Ord JK, Getis A. Local Spatial autocorrelations statistics: distributional issues and application. Geogr Anal. 1995 Oct;27(4):286–306.

10. Tsiampalis T, Panagiotakos DB. Missing-data analysis: Socio- demographic, clinical and lifestyle determinants of low response rate on self- reported psychological and nutrition related multi- item instruments in the context of the ATTICA epidemiological study. BMC Med Res Methodol. 2020 Jun;20(1):148.

11. Keys A, Aravanis C, Blackburn HW, Van Buchem FS, Buzina R, Djordjević BD, et al. Epidemiological studies related to coronary heart disease: Characteristics of men aged 40-59 in seven countries. Acta Med Scand Suppl. 1966;460:1-392.

12. Moulopoulos SD, Adamopoulos PN, Diamantopoulos EI, Nanas SN, Anthopoulos LN, Iliadi-Alexandrou M. Coronary heart disease risk factors in a random sample of Athenian adults. The Athens Study. Am J Epidemiol. 1987 Nov;126(5):882-92.

13. Seo S, Choi S, Kim K, Kim SM, Park SM. Association between urban green space and the risk of cardiovascular disease: A longitudinal study in seven Korean metropolitan areas. Environ Intern. 2019;125:51–7.

14. Bianconi A, Longo G, Coa AA, Fiore M, Gori D. Impacts of Urban Green on Cardiovascular and Cerebrovascular Diseases—A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2023 May;20(11):5966.

15. Li J, Siegrist J. Physical activity and risk of cardiovascular disease—A Meta-Analysis of Prospective Cohort Studies. Int J Environ Res Public Health. 2012 Jan;9:391–407.

16. Hartig T, Mitchell R, de Vries S, Frumkin H. Nature and Health. Annu Rev Public Health. 2014;35:207–28.