Environment and Health Fund

Grants & Fellowships

Collection of Abstracts

2008–2014

הקרן לבריאות וסביבה

Environment and Health Fund

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About the Environment and Health Fund

The Environment and Health Fund (EHF) is committed to expanding expertise in and knowledge about environmental health in Israel. EHF builds capacity and capabilities by supporting inter-disciplinary research, in-service professional training, and workshops and conferences. EHF helps connect Israeli scientists and policy makers to a network of international experts in environmental health research and policy.
EHF works with scientists and professionals, government and the private sector to broaden stakeholder involvement in reducing exposure to environmental hazards and improving public health.

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Introduction

Bridging two very different scientific domains to forge a new discipline is a daunting challenge. One of the primary goals of the Environment and Health Fund (EHF) has been the promotion of interdisciplinary research and training in environmental health in Israel. The 56 abstracts included in this volume are indicative of the breadth of this interdisciplinary field. Reviewing the research included here, we see the variety of environmental exposures of concern, along with the many health endpoints they influence. The complexity of promoting interdisciplinary research and training becomes even greater when one considers the methodological differences between research in environmental sciences as compared to epidemiological studies of human health and disease.

The more we learn about the increasing rates of chronic illnesses, the more we understand the importance of environmental factors. The scientific research that aids in unraveling these complex relationships is critical to our ability to appropriately intervene to reduce exposures and improve public health. We are proud to note that since its establishment in 2007, EHF has been a pioneer in Israel, establishing University Centers of Excellence, supporting interdisciplinary research, sending young Israeli scientists overseas to train in the most prestigious laboratories in the world, and most recently, assisting them to reintegrate into the field of environmental health research and training in Israel. As the community of environmental health researchers in Israel strengthens its ties to the global network of scientists and practitioners, our hope is that the sustainability of what has been accomplished thus far will be guaranteed.

Thanks are due to the staff and the board of the Environment and Health Fund for the efforts invested in the grants and fellowships programs, and in the production of this publication. Particular thanks are due to Dr. Sari Rosen whose work on every aspect of the grants and fellowships programs is performed with meticulous attention to detail and the highest standards of excellence.

The research outlined in this volume, and over 90 publications it produced, is evidence of the progress that has been made in establishing high quality research and training in environmental health in Israel. It is the first step towards building capacity. The Environment and Health Fund, along with the community of environmental health scientists and practitioners, remains committed to continuing to expand capabilities in order to allow us to meet present and future environmental health challenges.

Prof. Ilan Chet
Chairman

Dr. Ruth Ostrin
Director

Table of Contents

List of Grants & Fellowships 4

Data & Trends 9

University Centers of Excellence 13

Research Grants

- Multi-Year Research Grants 17
- Pilot Research Grants 32
- Small Research Grants 35
- Research Grants for Returning Post-Doctoral Fellows 39

Fellowships

- Post-Doctoral Fellowships 41
- Doctoral Fellowships 57

Index

- Investigators 62
- Topics 64

List of Grants & Fellowships

Multi-Year Research Grants

Reclaimed Wastewater and Sludge as Sources for Pharmaceutical Compounds: Fate in Soil and Groundwater 17
Benny Chefetz, Brian Berkowitz, Ishai Dror, Yitzhak Hadar

Characterization and Source Apportions of Local and Foreign $PM_{2.5}$ in Israel Under Different Synoptic Conditions 18
Yigal Erel, Uri Dayan, James Schauer, Levana Kordova, Arye Wanger

Identification, Isolation and Epidemiological Study of the Invasive Human Pathogen, *Vibrio Vulnificus*, from Water Resources 19
Yechezkel Kashi, Meir Broza, Hannah Sprecher, Ruti Yishai

Prevalence, Extent and Geographical Distribution of Asthma and Atopic Diseases in Young Adults in Israel and the Relationship with Air Quality 20
Yinon Rudich, Jeremy Sarnat, Arnon Afek, Shlomo Moshe, Ron Frimer, Alon Peretz, Nili Greenberg

Organophosphates in the Hula Basin: Atmospheric Levels, Transport, Degradation Products and Neurotoxic Hazards in Children Following Low-Level Long-Term Exposure 21
Yoram Finkelstein, Yael Dubowski, Michal Segal-Rosenhaimer, Eliyakim Doitsch, Elihu Richter

Chronic Exposure to Air Pollution and Long-Term Outcomes after First Acute Myocardial Infarction: A Population-Based Cohort Study 22
Yariv Gerber, Silvia Koton, David Broday, David. M. Steinberg, Yaacov Drory

Assessing Exposure to Selected Environmental Pollutants in the Israeli Population 23
Itamar Grotto, Tamar Berman, Rebecca Goldsmith, Yona Amitai, Tamy Shohat

Effect of Treated Wastewater Irrigation on Antibiotic Resistance in Agricultural Soil Bacteria 24
Eddie Cytryn

Childhood and Adolescent Environmental Exposures, Measures of Health Status at Age 17 and the Incidence of Cancer in Adulthood 25
Jeremy D. Kark, Joel Schwartz, Noam Levin, Hagai Levine, Ilan Levy, Lital Keinan-Boker

Formation of Environmental Health Policy in a Contested Science Environment 26
Oren Perez, Adi Ayal, Nadav Davidovitch, Ronen Hareuveny

Soils as a Source for Atmospheric Particles: Spatio-Temporal Impact on Air Quality and Human Health in the Negev 27
Itzhak Katra, Victor Novack, Lone Avnon, Dan Blumberg, Michael Friger, Petros Koutrakis

The Possible Association between Exposure to Air Pollution and Adverse Pregnancy Outcomes 28
Liat Lerner-Geva, Eli Stern, Yinon Rudich, Adel Farhi, Itzhak Benenson

Impact of Exposure to Brominated Flame Retardants (BFRs) and Phthalates on Birth Outcomes in an Israeli Cohort 29
Matitiahu Berkovitch, Dror Mandel, Pam Factor-Litvak, Joseph Tobvin, Tamar Berman, Malka Britzi, Stefan Soback, Amalia Levy, Ronit Lubetzky

The Exposure of Pregnant Women and their Offspring to Endocrine Disrupting Chemicals and Organophosphate Pesticides 30
Ronit Calderon-Margalit, Ronit Haimov-Kochman, Tamar Berman, Zivanit Ergaz-Shaltiel

Leveraging Telemedicine to Assess Associations between Acute Cardiovascular Events and Ambient Particulate Air Pollution in the Tel Aviv and Haifa Metropolitan Areas 31
Ronit Nirel, Alon Peretz, Uri Dayan, Sara D. Adar

Pilot Research Grants

Quantitative Evaluation of Organophosphate Pesticides and their Metabolites on Edible Crops 32
Benny Chefetz, Tamar Berman, Julius Ben-Ari, Yehoshua Maor, Dana Boyd Barr

Lung-on-Chip Alveolar Models for Inhaled Particle Cytotoxicity in Alveolar Epithelial Cells 32
Josué Sznitman, Barbara Rothen-Rutishauser, Peter Ertl

Endocrine Disrupting Chemical Burden among Residents of a Vegan-Organic Rural Community: The Amirim Study 33
Karen Tordjman, Tamar Berman, Thomas Göen

Evaluation of Adverse Health Effects in the Israeli Population from Lack of Magnesium and Iodine in Drinking Water from Desalinized Sea Water 33
Yona Amitai, Meital Shlezinger, Michael Shechter, Maya Leventer-Roberts

Mortality Related to Traffic Air Pollution in a Vulnerable Population: A Contemporary Experience with a Novel Exposure Model 34
Yariv Gerber, David Broday, David M. Steinberg

Establishing a Station to Evaluate and Enhance Satellite-Based Estimates of Ground-Level $PM_{2.5}$ Levels for Health Applications in Israel 34
Yinon Rudich, Ilan Koren

Small Research Grants

Distributed Low Cost Mobile and Wireless Sensor Network for Air Quality Monitoring with Applications to Traffic Related Urban Air Pollution 35
David Broday

Phthalate Concentration in Child Use and Care Articles: Preliminary Screening of the Israeli Market 35
Jenny Gun, Ovadia Lev

Biological Monitoring of Ultrafine Particles in the Airways of Asthmatic Children 36
Shira Benor, Shmuel Kivity, Elizabeth Fireman

Exposure to Air Pollution and Long-Term Incidence of Frailty after Myocardial Infarction: A Pilot Study 36
Yariv Gerber, David Broday, Vicki Myers, Yaacov Drory

Assessment of Young Children's Exposure to Hazardous Chemicals Especially Neurotoxins, in Pre-Schools, Kindergartens and Homes in Northern Israel 37
Debby Mir, Yoram Finkelstein, Igal Bar-Ilan, Elyakim Doitsch

Environmental Health Policy: Inter-Agency Aspects at the Government Level 37
Maya Negev

The Association of Air Pollution and Blood Glucose Levels Among Patients with Diabetes in the Negev Region 38
Victor Novack, Itai Kloog, Idit F. Liberty, Maayan Yitshak Sade

Monocytes and Macrophages as Integrators of Environmental Particles Exposure and Adipose-Derived Factors: Relevance to Adipose Inflammation in Obesity 38
Assaf Rudich, Yinon Rudich, James Schauer

Research Grants for Returning Post-Doctoral Fellows

Estimating Intra-Urban Exposure Patterns to Traffic-Related Pollution with a Distributed Sensors Network 39
Ilan Levy, David Broday, Barak Fishbain

Chemical Exposure, Granulosa Cell Exosomes, and Oocyte/Embryo Quality 39
Ronit Machtinger, Andrea Baccarelli, Russ Hauser, Catherine Racowsky

Post-Doctoral Fellowships

Characterization of Urban to Neighborhood Scale Air Pollutant and Human Exposure using a Comprehensive Array of Fixed and Mobile Measurement Platforms 41
Ilan Levy, Environment Canada, with Jeffrey Brook

Assessment of Dietary Exposure to Methylmercury and Polyunsaturated Fatty Acids through Fish Consumption and the Association with Cardiovascular Health 42
Shirra Freeman, Harvard University, with James K. Hammitt

Particle Exposure Assessment 43
Alexandra Chudnovsky, Harvard University, with Petros Koutrakis

Assessing Temporally-and Spatially-Resolved $PM_{2.5}$ Exposures for Epidemiological Studies Using Satellite Aerosol Optical Depth 44
Itai Kloog, Harvard University, with Joel Schwartz

Molecular Epidemiology of Lung Function: an Integrated Approach 45
Iris Lavi, CREAL, with Stefano Guerra

The Effect of BPA on Human Oocyte Maturation – In Vitro Study 46
Ronit Machtinger, Harvard University, with Catherine Racowsky and Russ Hauser

Breast Cancer and Epigenetics 47
Neomi Vin-Raviv, Columbia University, with Mary Beth Terry

Traffic-Related Air Pollution and Noise and Blood Pressure of Children: Results from the PIAMA Birth Cohort Study 48
Natalya Bilenko, Utrecht University, with Bert Brunekreef

In Utero and Early Childhood Pesticide Exposure and Respiratory Symptoms and Lung Function in Children 49
Rachel Raanan (Arnon), University of California, Berkeley, with Brenda Eskenazi

Association between Air Pollution and Incidence of Autism Spectrum Disorder in the Nurses' Health Study II 50
Raanan Raz, Harvard University, with Marc Weisskopf

Birth and Childhood Weight and Environmental Exposures 51
Keren Agay-Shay, CREAL, with Martine Vrijheid , Mark Nieuwenhuijsen and Jordi Sunyer

Traffic Related Air Pollution and Acute Health Response – Evidence from Panel-Based Studies 52
Rachel Golan, Emory University, with Jeremy Sarnat

Association of Long-Term Exposure to Air Pollution and Noise with Neurocognitive Functions in the Heinz Nixdorf Recall Study Cohort 53
Lillian Tzivian, IUF Leibniz Research Institute for Environmental Medicine, with Barbara Hoffmann

The Polybrominated Biphenyl (PBB) Cohort 54
Tamar Wainstock, Emory University, with Michele Marcus

Male Fertility and Environmental Exposures 55
Hagai Levine, Mount Sinai Hospital, with Shanna Swan

Metabolomics and Adductomics Analysis of Dried Blood Spots (DBS) from the Northern California Childhood Leukemia Study (NCCLS) 56
Lauren Petrick, University of California, Berkeley, with Stephen Rappaport

Doctoral Fellowships

Congenital Malformations and Associations with Ambient Air Pollution in Israel, 2000-2006 57
Keren Agay-Shay, University of Haifa

Study of the Relationship between Spatial Dispersion of Ischemic Heart Diseases and Respiratory Diseases and Meteorological, Vehicular Air Pollution and Socio-Economic Factors in Israel's Negev Region 57
Aliza Drory, Ben-Gurion University of the Negev

Multicultural Public Participation in Health Impact Assessment 58
Maya Negev, Ben-Gurion University of the Negev

Early Fetal Loss: The Association between Air Pollution and other Major Risk Factors and Spontaneous Abortions in Southern Israel 58
Riki Krispel-Ochayon, Ben-Gurion University of the Negev

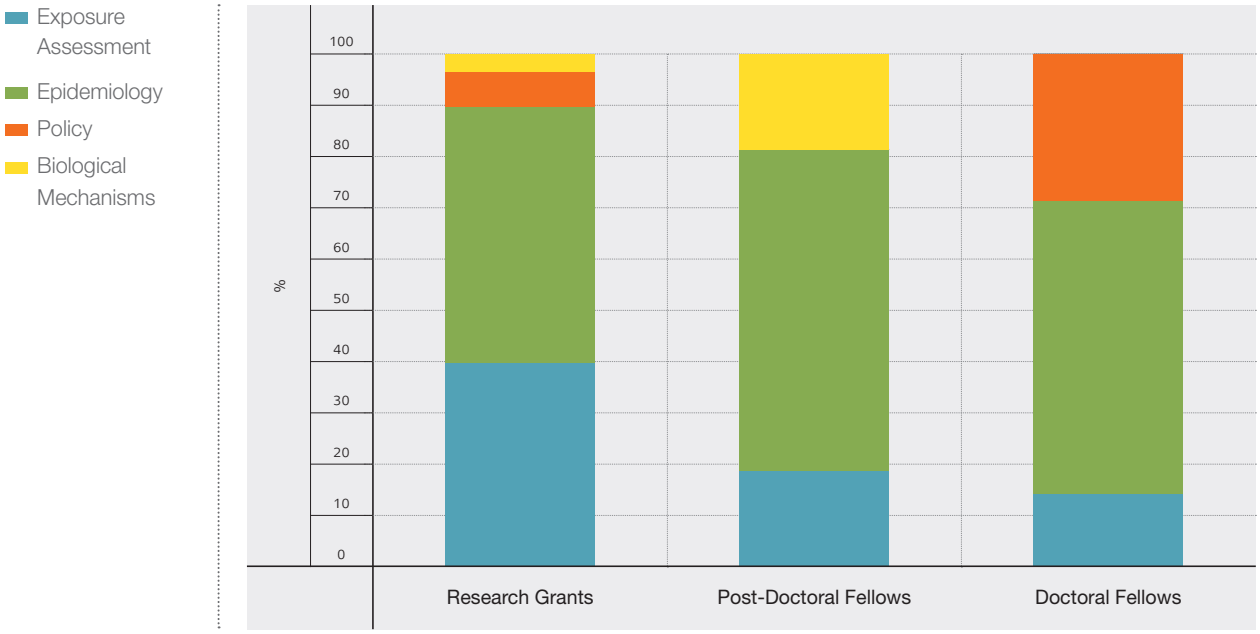
Understanding Policy Change Sequences in Vehicle and Industrial Air Pollution Policies in Israel 59
Ehud Segal, The Hebrew University of Jerusalem

Estimating Cancer Risk Attributed to Living in Proximity to Large Petroleum Storage Tanks 59
Marina Zusman, University of Haifa

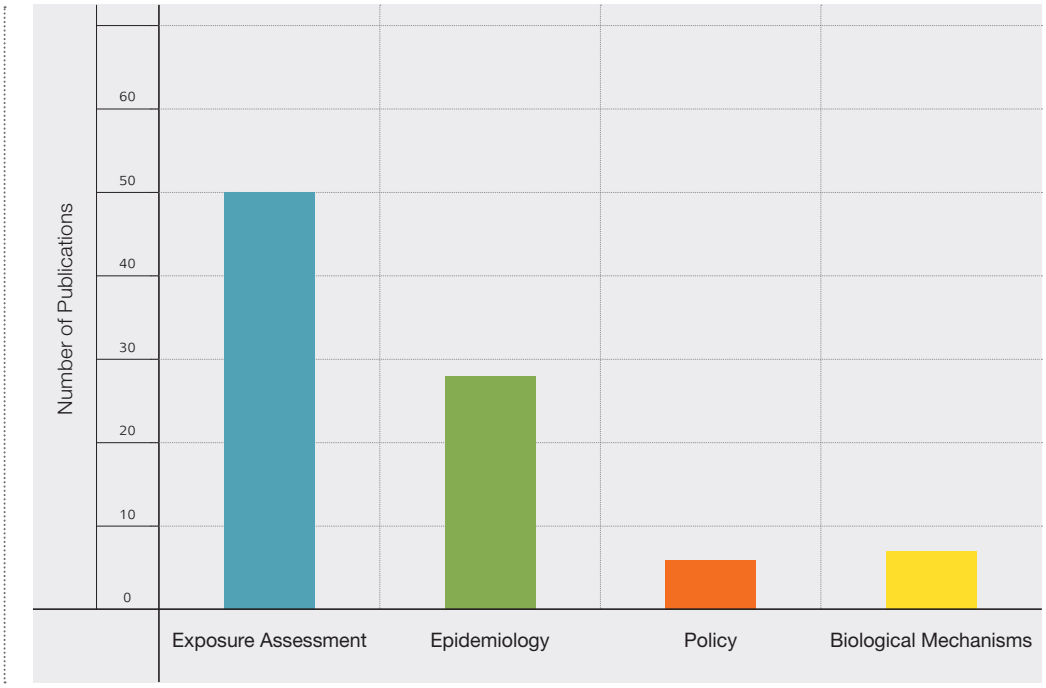
Integration of Satellite Observations and Ground Monitoring and its Application for Assessing Exposure to PM in Israel 60
Meytar Sorek-Hamer, Technion - Israel Institute of Technology

Data & Trends

Grants and Fellowships by Research Domain

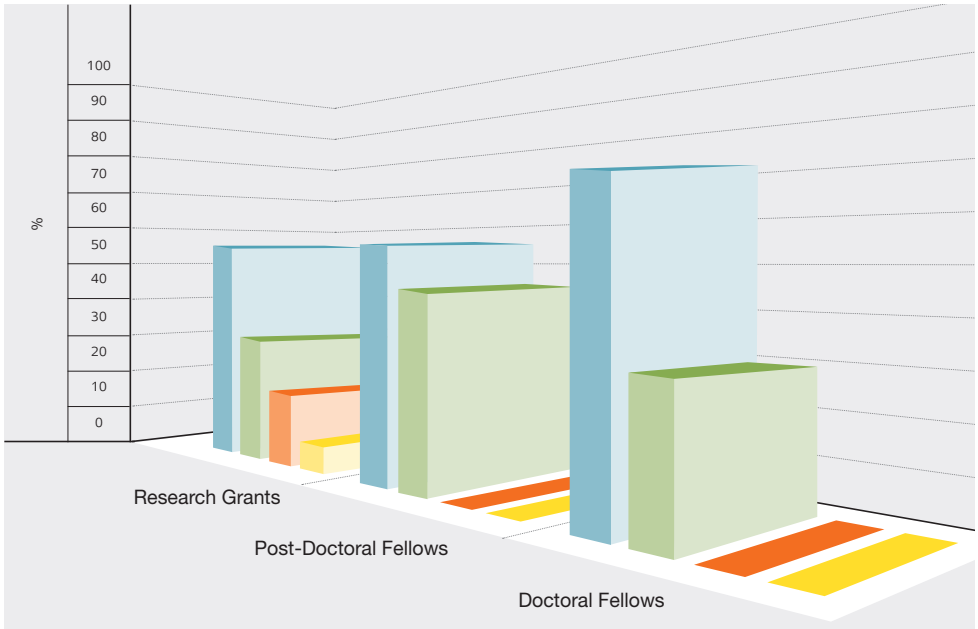


Publications by Research Domain for Grantees and Fellows



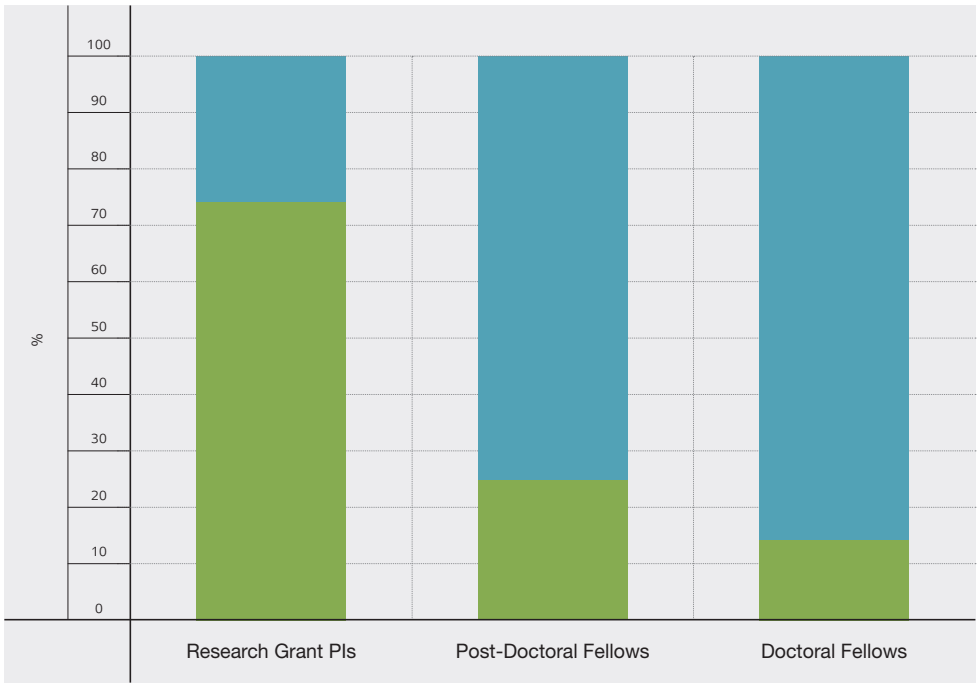
Grants and Fellowships by Pollution Source

- Air
- Multiple sources (incl. food and consumer products)
- Water
- Non-Ionizing Radiation

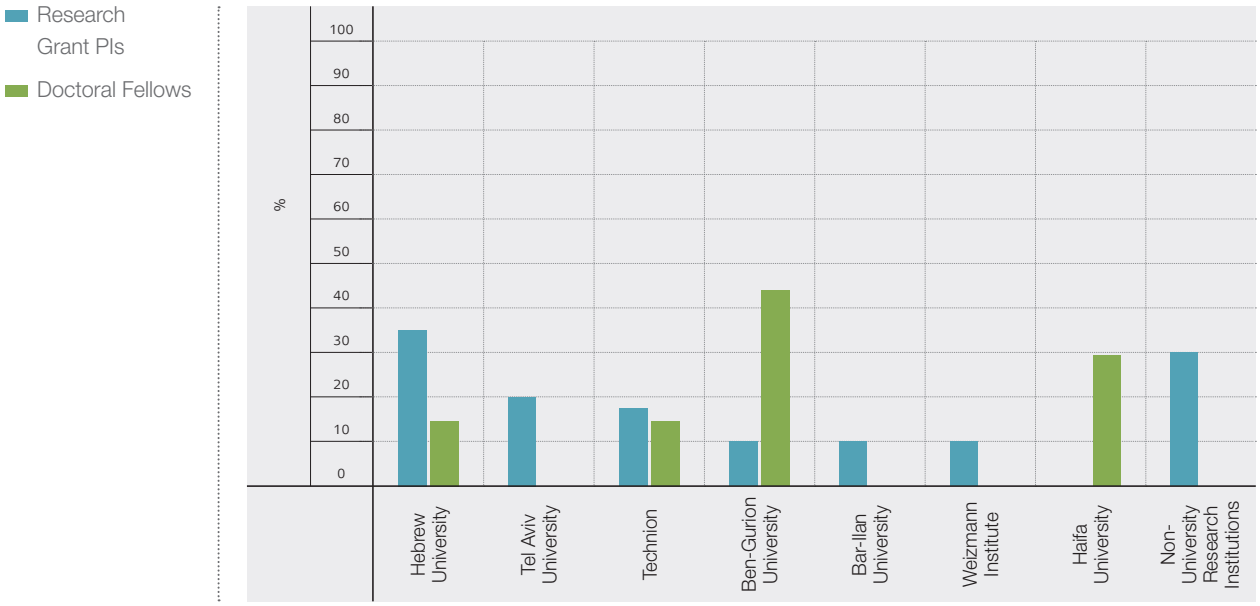


Grants and Fellowships by Gender

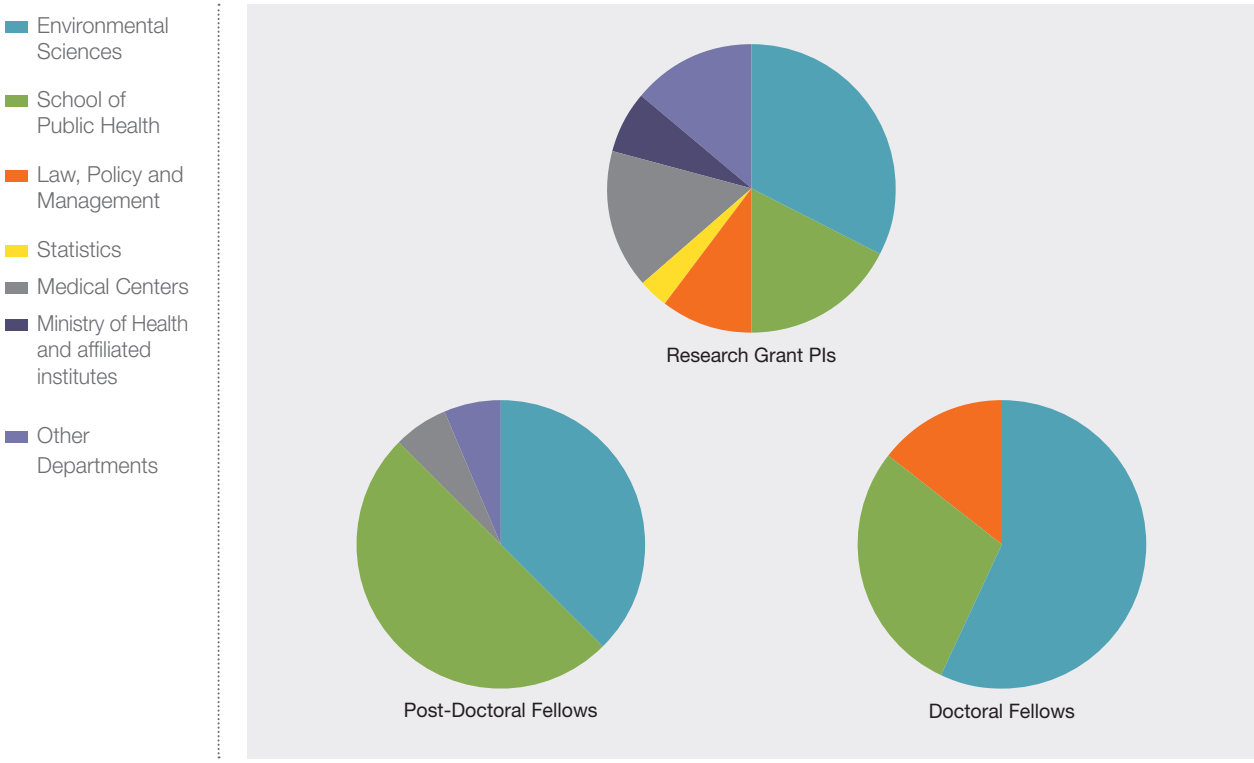
- Female Researchers
- Male Researchers



University Affiliation



Department or Institutional Affiliation



University Centers of Excellence

Technion Center of Excellence in Exposure Science and Environmental Health

Director
David Broday

Members
Yael Dubowski
Barak Fishbain
Abraham Reznick
Yuval Zudman
Ilan Levy

Scientific Coordinator
Yael Etzion

The Technion Center of Excellence in Exposure Science and Environmental Health (TCEEH) was established in 2011 as a joint collaboration between the Technion's Faculty of Civil and Environmental Engineering and the Ruth and Bruce Rappaport Faculty of Medicine.

TCEEH research focuses on understanding human exposure to relevant air pollutants, and the biological responses that follow this exposure. Due to population growth, industrialization, and urbanization, the Israeli public is exposed to high levels of air pollutants, experiences deteriorating urban air quality, suffers from reduced visibility and from increasing frequency of photochemical smog episodes, and faces aggravating warming and drought due to both urban heat island effects and climate changes. The global trend of improved standards of living and Israel's distinct national situation (political, military, economic, etc.) and unique geo-meteorological conditions contribute, and oftentimes synergistically exacerbate, environment-health relationships. Moreover, on top of these dynamic conditions the close proximity between people (the receptors) and pollutant sources gives rise to unique circumstances. In these circumstances Israelis are routinely exposed to mixtures of anthropogenic and biogenic, fresh and aged, organic and inorganic, urban and rural/agricultural, and toxic and harmless respirable pollutants. The Center, through its research cores, addresses these issues by promoting research on priority pollutants and in relation to aggregate exposure scenarios.

The Center's ongoing projects include:

- CITI-SENSE - Development of sensor-based Citizens' Observatory Community for air pollution measurement and exposure estimation
- IT and video based estimation of exposure to traffic related pollutants
- Assessment of primary and secondary pesticide drift under sub-humid climate; field measurements and modeling approaches
- Decontamination of toxic residues on surfaces via in situ photo-oxidation
- Remote sensing of airborne particulate matter via both satellite-borne and ground measurements
- Development of a comprehensive national air quality monitoring database that covers observations since the late 90's
- Modeling ambient concentrations of, and exposure to, respirable pollutants, especially in urban areas

The Center's activities benefit from the input of an international Scientific Advisory Committee (SAC) comprising leading researchers in the fields of exposure science and environmental health:

- Jeremy Sarnat, SAC Chair, Rollins School of Public Health, Emory University, USA
- Petros Koutrakis, School of Public Health, Harvard University, USA
- Michael Brauer, School of Population and Public Health, University of British Columbia, Canada
- James Schauer, Department of Civil and Environmental Engineering, University of Wisconsin-Madison, USA
- Mark Nieuwenhuijsen, Center for Research in Environmental Epidemiology (CREAL), Barcelona, Spain

Hebrew University Center of Excellence in Agriculture and Environmental Health

Director
Benny Chefetz

Members
Orly Manor
Ora Paltiel
Zvi Roth
Ronit Calderon-Margalit
Tamar Berman
Hagai Levine

Coordinator
Yehoshua Maor

The Hebrew University Center of Excellence in Agriculture and Environmental Health was established in 2012 as a collaboration between the Robert H. Smith Faculty of Agriculture, Food and Environment and the Braun School of Public Health and Community Medicine, along with colleagues from the Ministry of Health.

In Israel, where almost all arable land is currently intensively farmed and water resources are being over-utilized, the risks of exposures and adverse health effects from agricultural activities are high. Moreover, the risks are magnified because much of Israeli farming takes place in close proximity to population centers. This enhances the direct and indirect effects of agriculture on the surroundings municipalities. Israel is also unique and a pioneer in recycling wastewater for agriculture use. In order to overcome the shortage of water, Israeli agriculture relies heavily on reclaimed wastewater (i.e., treated effluents) as an important source of irrigation water. The Center's mandate is to explore the interface between modern agricultural activity, environmental quality and human health through multidisciplinary research, dissemination and outreach. The consortium of environmental scientists and public health researchers aims to encourage multidisciplinary research activities, enhance public awareness, minimize the effects of agricultural activities on the environment, and better understand the consequences of agro-activities on human health.

The Center's current projects include:

- Xenobiotics originating from reclaimed wastewater: Uptake by crops and exposure assessment
- Bioaccumulation of endocrine disrupting chemicals by dairy cows via consumption of crops irrigated with reclaimed wastewater
- Serum carbamazepine levels among healthy Israeli volunteers
- Exposure of Israeli children to pesticides via food consumption
- Exposure of pregnant women and their offspring to endocrine disrupting chemicals and organophosphate pesticides and associations with fetal growth and development of reproductive organs
- Pesticide exposure and reproductive health outcomes in Palestinian and Israeli male residents of Jerusalem

The Center's activities benefit from the input of an international Scientific Advisory Committee (SAC) comprising leading researchers in the fields of exposure science and environmental health:

- Brenda Eskenazi, SAC Chair, School of Public Health, University of California, Berkeley, USA
- Shanna Swan, School of Medicine, Mount Sinai Hospital, New York, USA
- Baoshan Xing, Environmental & Soil Chemistry Program, University of Massachusetts, Amherst, USA
- Leslie Stayner, School of Public Health, University of Illinois at Chicago, USA
- Yitzhak Hadar, Robert H. Smith Faculty of Agriculture, Food and Environment, Hebrew University of Jerusalem

Research Grants

Reclaimed Wastewater and Sludge as Sources for Pharmaceutical Compounds: Fate in Soil and Groundwater

Benny Chefetz[1]
Brian Berkowitz[2]
Ishai Dror[2]
Yitzhak Hadar[1]

1. The Hebrew University of Jerusalem
2. Weizmann Institute of Science

2008–2012

Current understanding of the fate of pharmaceutical compounds (PCs) in the soil-water environment is highly limited. In this project we focus on three principal, inter-related aspects: sorption interactions, degradability, and migration behavior of PCs in the soil-water environment. The main objectives of the proposal were to evaluate: (1) the behavior of PCs in top-layer soil; (2) migration behavior of PCs, assessing the threat of PC release to groundwater quality; and (3) the biodegradability of PCs in treated wastewater-irrigated soils. The sorptive behavior and mobility of PCs in the top soil layer were studied in column experiments and biodegradation was studied in microcosms.

Our data suggest that application of biosolids to agricultural soil may result in greater retardation of PCs in the top layer of the soil; however, the mobility of more polar and water soluble PCs may not be affected by the addition of biosolids. Solution chemistry (i.e., irrigation with reclaimed wastewater) can alter the behavior of PCs in the top-soil profile: the high pH level of treated wastewater enhances the mobility of PCs that classify as weak organic acids, and high concentrations of dissolved organic matter (DOM) may also enhance mobility of PCs. Regarding the latter point, the ratio of DOM:PC in the solution must be relatively high to facilitate PC-DOM interactions.

Our data obtained from microcosm experiments show that carbamazepine (CBZ) is highly stable in soils with $t_{1/2}$> 300 days. All other tested PCs were found to degrade in the soils, without significant differences between soils that were irrigated with treated wastewater or fresh water. Due to the high persistence of CBZ, we evaluate the possibility that pure culture of the white-rote fungus Pleurotus ostreatus is capable of degrading this compound. Our data show high efficiency of P. ostreatus to remove CBZ from solution using both manganese peroxidase and cytochrome p-450 monooxigenase enzymes.

Data obtained from this project suggest that active PCs introduced to the environment via irrigation with reclaimed wastewater and/or sludge application are relatively persistent; thus, they have the potential to contaminate water resources and be retained in the top soil layer.

Research publications

(1) Arye, G., Dror, I., & Berkowitz, B. (2011). Fate and transport of carbamazepine in soil aquifer treatment (SAT) infiltration basin soils. *Chemosphere, 82*(2), 244-252.

(2) Golan-Rozen, N., Chefetz, B., Ben-Ari, J., Geva, J., & Hadar, Y. (2011). Transformation of the recalcitrant pharmaceutical compound carbamazepine by Pleurotus ostreatus: Role of cytochrome P450 monooxygenase and manganese peroxidase. *Environmental Science & Technology, 45*, 6800–6805.

(3) Navon, R., Hernandes-Ruiz, S., Chorover, J., & Chefetz, B. (2011). Interactions of carbamazepine in soil: Effects of dissolved organic matter. *Journal of Environmental Quality, 40*, 942-948.

(4) Borgman, O., & Chefetz, B. (2013). Combined effects of biosolids application and irrigation with reclaimed wastewater on transport of pharmaceutical compounds in arable soils. *Water Research, 47*, 3431-3443.

(5) Grossberger, A., Hadar, Y., Borch, T., & Chefetz, B. (2014). Biodegradability of pharmaceutical compounds in agricultural soils irrigated with treated wastewater. *Environmental Pollution, 185*, 168-177.

Characterization and Source Apportions of Local and Foreign $PM_{2.5}$ in Israel Under Different Synoptic Conditions

Yigal Erel[1] | Uri Dayan[1]
James Schauer[2]
Levana Kordova[3] | Arye Wanger[4]

1. The Hebrew University of Jerusalem
2. University of Wisconsin-Madison, USA
3. Israel Ministry of Environmental Protection
4. Adam Teva VaDin (IUED)

2008–2012

The Middle East is one of the regions in the world where relatively high concentrations of atmospheric particulate matter (PM) have been detected frequently. It has been suggested that PM levels in the Middle East are present at levels that lead to adverse health effects and to poor visibility.

The hypothesis underlying this study is that the integration of meteorological conditions with detailed characterization of aerosol composition and sources is crucial for the evaluation of the health effect of aerosols and for developing strategies and standards to protect the public from air pollution. The two research aims were: (1) to develop source receptor relationships for $PM_{2.5}$ in Israel that can be related both to the physical origin of sources and specific sources for local air pollution; and (2) to understand how meteorological analysis of air pollution can sufficiently classify air pollution sources and composition to provide a cost effective metric to use in epidemiological studies.

The synoptic conditions prevailing in Israel allowed us to characterize the composition and properties of atmospheric PM. This was done in conjunction with detailed analysis of air masses movements and transport models. In the summer, during Persian Trough conditions PM concentrations are lowest, the ratio of $PM_{2.5}/PM_{10}$ is highest, the spatial and temporal variations are relatively low, and toxic metal concentrations (As, V) are highest. In contrast, during dust storms prevailing in the fall, in the spring, and in the winter PM concentrations vary a lot, $PM_{2.5}/PM_{10}$ ratio is lowest, and most of the toxic metals are from urban sources located en-route of the air masses. From a public health perspective, our finding highlights the fact that in Israel when PM concentrations are lowest their health impact is not necessarily low because of their higher toxicity levels.

In order to minimize the adverse public health effects of atmospheric PM by exposure management, there is a need for a greater understanding of mechanisms of atmospheric PM toxicity. For this purpose bioassay techniques were utilized and a reporter panel of 10 genetically engineered bacterial (Escherichia coli) strains was composed. Each panel member was designed to report on a different stress condition with a measurable light signal produced by the luciferase enzyme. The reporter panel approach, as demonstrated in this study's results, has the potential of providing novel insights as to the mechanisms of atmospheric PM toxicity. Furthermore, combining the panel's results with bioavailability data can enlighten the role of different PM components in the observed toxicity.

Research publications

(1) Dayan, U., Erel, Y., Shpund, J., Kordova, L., Wanger, A., & Schauer, J.J. (2011). The impact of local sources and meteorological factors on nitrogen oxide and particulate matter concentrations: A case study of the Day of Atonement in Israel. *Atmospheric Environment, 45*, 3325-3332.

(2) Kessler, N., Schauer, J., Yagur-Kroll, S., Melamed, S., Tirosh, O., Belkin, S., & Erel, Y. (2012). A bacterial bioreporter panel to assay the cytotoxicity of atmospheric particulate matter. *Atmospheric Environment, 63*, 94-101.

(3) Erel, Y., Tirosh, O., Kessler, O., Dayan, U., Belkin, S., Stein, M., Sandler, A., & Schauer, J.J. (2013). Atmospheric particulate matter (PM) in the Middle East: Toxicity, trans-boundary transport, and influence of synoptic conditions. In P. Censi, T.H. Darrah, & Y. Erel (Eds.), *Medical geochemistry - geological materials and health*. Springer.

Identification, Isolation and Epidemiological Study of the Invasive Human Pathogen, *Vibrio Vulnificus*, from Water Resources

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Meir Broza[2]
Hannah Sprecher[3]
Ruti Yishai[4]

1. Technion – Israel Institute of Technology
2. University of Haifa - Oranim
3. Rambam Health Care Campus
4. Israel Ministry of Health

2008–2012

Vibrio vulnificus is a worldwide highly invasive human pathogen, with one of the highest mortality rates. Human infections are acquired through consumption of contaminated seafood or through skin wounds. It is considered as an important emerging environmental and food safety issue around the world. Strains of *V. vulnificus* are divided into three different biotypes. The highly virulent Biotype 3 was isolated until now only in Israel and is responsible for numerous infections each year. Our recent genomic study suggests the existence of an additional new virulent group, clade A.

The objective of the research was to follow the route of contamination of the water associated pathogen, *V. vulnificus* in Israel. The heterogeneity of the bacterial population in different water bodies was studied through genomic diversity in comparison with clinical samples. We developed rapid identification and typing method based on three technologies; SSR molecular markers, MLST and on a custom genome-wide single nucleotide polymorphisms (SNP) genotyping array. 254 clinical and environmental isolates with worldwide distribution recovered over a 30-year period were successfully genotyped by the array. This powerful high-throughput approach enabled us to simultaneously cover 570 SNPs randomly distributed throughout the entire genome of *V. vulnificus* among a diverse and large number of isolates.

Our data demonstrate that the developed SNP genotyping technology could be utilized for accurate strain identification, for inferring phylogenetic relationships among strains and for epidemiology studies. Analyses of the array data together with our recently draft genome sequence of biotype 3 strain VVyb1(BT3), suggest that biotype 3 as created bade on biotype 1 genome that gained rather small number of genes from other bacterial species sharing the same niche, e.g., Shewanella. Results support the recent emergence of new pathogenic groups (clade A) within this species as a recurrent phenomenon. These results emphasize the rapid genetic change of such pathogenic bacteria in their natural ecological niche, in this case artificial fish aquaculture farms in Israel. The results specifically contribute to the broad understanding of the evolution of this human pathogen. The ongoing intervention in environmental niches like these requires our continuous preparedness to cope with such emerging risks.

Research publications

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Prevalence, Extent and Geographical Distribution of Asthma and Atopic Diseases in Young Adults in Israel and the Relationship with Air Quality

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2008–2012

Background: Air pollution from mobile sources is associated with increasing asthma prevalence. In Israel, traffic is a major air pollution source. We conducted a retrospective cross-sectional study to evaluate the possible association and its extent between exposure to nitrogen oxides, markers of traffic-related air pollution and asthma prevalence in young adults in Israel.

Methods: A searchable database of air pollution in Israel was constructed for the years 1997-2008, based on information from the Ministry for Environmental Protection and the Israel Electric Company. The study included 36,874 young males who underwent the Israel Defense Forces (IDF) health examination and lived in one of twenty cities with at least one air monitoring station. We used half-hourly measurements of NO, NO_2, and NO_x. As proxy for cumulative lifetime exposures to traffic pollution, we examined 1-, 2-, and 3-year average NO, NO_2, and NO_x concentrations assigned to each subject based on city of residence and date of medical examination using logistic regression models, and accounting for other confounders.

Results: Physician-diagnosed asthma prevalence occurred in 6.5% of the subjects, 3.4% with active asthma and 3.1% with non-active asthma. Socio-demographic factors, birth country of father, birth country, cognitive abilities, education-level, body mass index, socio-economic status and number of children in the family, were also associated with asthma prevalence. After accounting for these factors we found high association of asthma with NO, NO_2 and NO_x exposure.

Conclusions: Consistent and significant positive associations were found between asthma prevalence and NO_x levels which are lower than the exposure standards set by environmental protection agencies. Among the active asthma group, odd ratios were considerably higher for NO_2 and NO_x than among the non-active asthma group, especially at the highest quintile of exposure. It is possible that residual confounding due to covariates that were not included in the current modeling approach may explain some of the observed findings regarding asthma prevalence.

Implications for Israel: The NO_x pollution standard in Israel is high (as in other countries). Our results suggest that the standards should be lower in order to reduce asthma prevalence.

Organophosphates in the Hula Basin: Atmospheric Levels, Transport, Degradation Products and Neurotoxic Hazards in Children Following Low-Level Long-Term Exposure

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2009–2013

Organophosphate pesticides (OPs) have been widely used in the Hula Valley. A significant portion of applied OPs remains suspended in the atmosphere despite the low volatility. This project assessed the effect of low-level long-term OP exposure on children and atmospheric levels of key OPs in the valley. Previous studies (1977-87) showed in-season reversible neurobehavioral effects of OP exposures in residents of kibbutzim in the valley. This cross-sectional study assessed neurobehavioral outcomes in 8-12 year-old schoolchildren (n=135) divided into subgroups: (1) those who reside and study in the Hula Valley (n=51), and (2) those who study in the valley but reside on the surrounding hills (n=45). In these two sub-groups 84% of the children are "second generation" of OP exposure, (3) a comparison group (n=39) of age- and sex-matched schoolchildren living in a different kibbutz in the Rift Valley where OPs have been minimally used for decades. Cognitive tests were performed. Saliva was sampled to measure paraoxonase-1 (PON1) gene polymorphisms. Urinary samples were collected in three consecutive spraying seasons to measure OP metabolites.

Results: An exposure-effect gradient was shown in cognitive tests including Trail B, Digit Symbol, Digit Cancellation A and Bender Gestalt tests, Purdue Pegboard in two sub-tests (in both hands and in the subdominant hand). Performance was inversely related to OP exposure in complex tests that contain scanning and manual dexterity elements. In parallel, atmospheric concentrations, transport and transformations processes of key OPs were studied. Measurements of airborne OPs in a few settlements adjacent to agricultural fields showed spatial and temporal variability; and also indicated that applied pesticides may reach nearby settlements during application (primary drift) and in the following few days (secondary drift). Maximal concentrations were observed during application. A non-steady-state atmospheric dispersion model (CALPUFF) was used in order to investigate pesticide transport within the valley during the studied application events. Model results successfully repeated the observed temporal trend but underestimated OPs air concentrations near field. In addition, laboratory studies of photo-oxidation of chlorpyrifos (a commonly used OP) adsorbed on various outdoor surfaces (soil, leaves and glass) were conducted to evaluate the impact of such surface processes on its environmental fate. The results provide better estimation of atmospheric levels of key OPs and their derivatives as well as new information on the health hazards of lengthy exposures to OP drift on children.

Research publications

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Chronic Exposure to Air Pollution and Long-Term Outcomes after First Acute Myocardial Infarction: A Population-Based Cohort Study

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2009–2012

Background: Epidemiological studies have provided broad evidence of the association between exposure to air pollution and cardiovascular disease (CVD) events. Long-term exposure to air pollution has been associated with progression of atherosclerosis, the underlying cause of CVD. Particulate air pollution appears to be the pollutant most consistently associated with adverse health outcomes, although associations have been reported also for NO_2 and traffic-generated pollutants. Preliminary data suggest that patients with myocardial infarction (MI) may be particularly vulnerable to the effects of chronic exposure to air pollution. However, methodological limitations inherent in the current literature, in addition to conflicting results, challenge these findings.

Objectives: Using a historical prospective study, we aimed to evaluate the associations of chronic exposure to air pollutants with the occurrence of clinical outcomes after MI during long-term follow-up; to assess the incremental value of air pollution exposure over individual-level demographic, socioeconomic, clinical variables, and neighborhood-level SES, in predicting morbidity and mortality post-MI. We hypothesized that chronic exposure to air pollutants would be independently associated with long-term adverse post-MI outcomes.

Major conclusions, solutions and achievements: A model assessing risk from chronic exposure to air pollutants was developed. High background levels of fine particulate matter ($PM_{2.5}$) were detected in central Israel, surpassing international guidelines. Furthermore, our findings demonstrate that chronic exposure to $PM_{2.5}$ has serious adverse health effects in post-MI patients in central Israel, increasing the risk of mortality and cardiovascular events.

Implications for environment and health in Israel: The results of this research provide evidence of the adverse health effects of elevated $PM_{2.5}$ levels in central Israel in heart patients. Study findings are based on high-quality data from a well-defined MI cohort with extensive information on various confounding factors, sufficient follow-up period, and multiple outcomes assessed longitudinally. Steps need to be taken to reduce the public health threat of PM pollution.

Research publications

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Assessing Exposure to Selected Environmental Pollutants in the Israeli Population

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2009–2013

Human biomonitoring (HBM) is used to estimate exposure to environmental chemicals by measuring the chemicals or their metabolites in tissues or body fluids (e.g., blood or urine). HBM is an important tool for determining the effectiveness of public health efforts to reduce public exposure to specific chemicals, for tracking time trends in exposure levels, and for determining whether exposure levels are higher among potentially vulnerable groups such as minorities and children. Therefore many countries have developed national biomonitoring programs. The objectives of the study were to test the hypothesis that levels of exposure (urinary concentrations) to several environmental contaminants in the Israeli population are different from those in US and European populations, and to test the hypothesis that diet is an important source of exposure to environmental contaminants in Israel.

The current study provided valuable data on exposure of the general population in Israel to a range of environmental contaminants, including organophosphate pesticides, bisphenol A, phthalates, environmental tobacco smoke, and polycyclic aromatic hydrocarbons. The study showed that exposure to several environmental contaminants (organophosphate pesticide, environmental tobacco smoke, phthalates) in the Israeli population is high compared to other international populations. Urinary bisphenol A concentrations were significantly higher in Jewish compared to Arab and Druze study participants and in current smokers. Total organophosphate metabolites were higher in study participants with high income compared to subjects with the lowest income and in study participants with high fruit consumption (>75th percentile). Exposure to environmental tobacco smoke was associated with being male, younger age, and low education status.

The major implications of the study for environment and health in Israel are: (1) Ministry of Health commitment to continue biomonitoring in the general population, including a plan to incorporate biomonitoring in the "MABAT" National Health and Nutrition Survey scheduled for 2015; (2) data to support policy aimed at reducing agricultural use of organophosphate pesticides in Israel; and (3) data to support policy aimed at reducing exposure to environmental tobacco smoke in non-smokers in Israel.

Research publications

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Effect of Treated Wastewater Irrigation on Antibiotic Resistance in Agricultural Soil Bacteria

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2010–2012

Antibiotic resistance (AR) is a global phenomenon with severe epidemiological ramifications. Anthropogenically-impacted natural environments can serve as reservoirs of antibiotic resistance genes (ARG), which can be horizontally transferred to human pathogens through water and food webs. Treated-wastewater (TWW) irrigation is widespread in arid regions of the world and especially in Israel (~50% of water used for agriculture), due to growing demand and diminishing freshwater supplies. However, wastewater effluents may contain residual concentrations of antibiotics, antibiotic-resistant bacteria (ARB), and ARGs, which can stimulate proliferation of AR in irrigated soil microcosms. To assess this hypothesis, we conducted comprehensive source tracking of ARB and ARGs in WWTP effluents and in freshwater- and TWW-irrigated soils; and determined the quantitative impact of residual levels of antibiotics on the abundance and diversity of ARB and ARGs in soil microcosms.

High levels of antibiotic resistance were detected in all soils analyzed; however, contrary to our hypothesis, ARB and ARG levels were identical in the TWW- and freshwater-irrigated soils, despite the fact that high levels of resistant bacteria and genes were found in the TWW that was used for irrigation. Bench-scale soil microcosms irrigated with different levels of the antibiotic ciprofloxacin, showed negligible differences in the microbial community composition and the levels of resistant bacteria in the soils even when antibiotic concentrations were an order of magnitude higher than concentrations traditionally found in wastewater effluents. This strongly suggests that residual concentrations of antibiotics from wastewater do not result in proliferation of antibiotic resistance in the soil microbiome. Collectively our results show that the high levels of AR bacteria and ARGs in both the freshwater- and the TWW-irrigated soils are indicative of high levels of native AR in natural soil microbiomes. Although more comprehensive research is necessary, our results suggest that irrigation with recycled water does not significantly increase ARG reservoirs in soil, and therefore are cause for cautious optimism. Future research in our lab will specifically focus on assessing mobile genetic elements that carry ARGs in both wastewater effluents and in native soils. These mechanisms are of significant epidemiological potential because they can be horizontally transferred to clinically-relevant bacteria.

Research publications

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Childhood and Adolescent Environmental Exposures, Measures of Health Status at Age 17 and the Incidence of Cancer in Adulthood

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2010–

We have developed an epidemiologic resource for assessing associations of environmental exposures in adolescence with multifaceted health outcomes that will focus initially on relating traffic air pollution exposure to measures of health status in adolescence and to subsequent cancer incidence and cause-specific mortality during young and mid adulthood.

Israelis undergo a compulsory health examination at the age of 17 prior to military service. We have linked ~2,600,000 males and females examined from 1967 to 2012 to the national cancer register to ascertain incident cancer diagnoses (n=63,000) and to the national death registry to ascertain cause-specific mortality outcomes (n=44,000) during follow-up periods extending up to 40+ years. We are geocoding the residential addresses at age 17 (i.e.. x,y geographic coordinates) in order to enable estimation of individual environmental exposures as well as census tract-based characteristics such as socioeconomic position. A Geographic Information Systems-based (GIS-based) reconstruction of the road system, built-up areas, population densities, traffic volumes and open spaces in Israel was undertaken for each decade going back from the present to the 1960s. These data served as the inputs for the development of NO_x-based land use regression models to predict monitoring station measures of traffic-related pollution exposure for the recent period (1990-2010). The models that were extrapolated back to the 1960s are being validated against independent estimates by the Central Bureau of Statistics of traffic-based pollution. The models are to be expanded to include $PM_{2.5}$ exposures. The main outcomes to be assessed are measures of health status at age 17 (as determined at the recruitment center health examinations) and subsequent incident site-specific cancer and cause-specific mortality. The study should soon enter the data analysis phase.

The reconstructed exposure estimates can, in the future, be further developed to accommodate additional environmental hazards such as electromagnetic fields produced by electric power lines and agricultural exposures to which the geocoded addresses can be linked.

Formation of Environmental Health Policy in a Contested Science Environment

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2010–

The objective of the proposed study is to assess the processes through which environmental and health regulations in Israel are devised and implemented in response to the emergence of new technologies, which are embedded in scientific uncertainty. Our particular focus will be on the regulation of cellular telephony and base antennas. We shall trace how the people and institutions involved in devising new regulation treat relevant scientific findings at early stages in which no scientific consensus has emerged. How are regulatory decisions made, we ask, when they are perforce based on contested science? The proposed study will employ different methodologies to examine the way in which environmental health policies have evolved in Israel in the context of these technologies, using in-depth legal analysis of the evolution of the current regulatory structures, extensive interviews of relevant stakeholders, structured questionnaires of public health physicians and epidemiological literature review. Because novel technologies (biotechnologies, nanotechnologies, digital technologies and others) are an important part of our economy and society, regulation in the face of scientific controversy will be an ever-mounting challenge in Israel and throughout the developed world.

Our study will be an important step towards improving the way such regulation is fashioned. Apart from contributing to the Israeli public health policy-making, the suggested study will complement other studies conducted mainly in the US and Europe which examine how regulators cope with uncertainty in the environment and health field.

Research publications

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Soils as a Source for Atmospheric Particles: Spatio-Temporal Impact on Air Quality and Human Health in the Negev

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2011–2014

Soils in arid and semi-arid zones are source areas for air pollution through emissions of dust-sized particles into the atmosphere. Although the association between environmental dust exposure and morbidity exists, our rudimentary understanding of the relationships between soil-derived airborne particles (SDAP), Chronic Obstructive Pulmonary Disease (COPD), and thus, socio-economic consequences, dictates the need for innovative and interdisciplinary quantitative-research into these issues. The overall objective of this research was to explore the impact of chronic and acute exposure to SDAP on COPD in space and time in the northern Negev. The Negev is located within the largest global dust belt and experiences several intensive dust storms every year. The unique setting in which all patients are treated by one hospital (Soroka) and one pulmonology clinic allows us to perform a population based analysis with no subjects lost to follow-up.

In the first phase of the project we established an epidemiological (population-based) association between dust storms and COPD exacerbations. The findings indicate that this arid urban environment experiences high PM_{10} levels whose origin lies in both local and regional dust events. During the study period daily PM_{10} concentrations reached over 2,000μg/m^3. An average daily net contribution of dust to PM_{10} of 122μg/m^3 was calculated for the entire study period which exceeds the WHO guideline (50μg/m^3). We found a positive association between dust storms and the rate of hospitalization for COPD exacerbation: (IRR=1.16, 95%CI, 1.08-1.24, $p<0.001$). The effect increased with age and was higher in women.

In the second phase we prospectively investigated the association between individual SDAP exposure and COPD parameters in the population of COPD patients. Real-time $PM_{2.5}$ and PM_{10} levels were measured simultaneously in outdoor and indoor environments over 14 dust events. The results demonstrate that during the climax of dust storms the spatial variations in PM can reach 400μg/m^3 between different locations in the city. Indoor PM_{10} and $PM_{2.5}$ levels reached very high concentrations of 1,855μg/m^3 and 566μg/m^3, respectively. More than 100 patients enrolled during the second phase. FEV1 values tend to be lower in dust storm days but the data are still being analyzed.

The findings of the project allow linking specific health situations to source and emission types, implementing methods for exposure and risk assessment (individual and group levels), and assimilating natural resource management into development activities. We anticipate that the outcome of the research will be helpful in creating interventions and policies designed to reduce the phenomena while enhancing the quality of life in the Negev.

Research publications

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(3) Vodonos, A., Friger, M., Katra, I., Avnon, L., Krasnov, H., Koutrakis, P., Schwartz, J., Lior, O., & Novack, V. (2014). The impact of desert dust exposure on hospitalization due to the exacerbation of chronic obstructive pulmonary disease. *Air Quality, Atmosphere and Health*. doi: 10.1007/s11869-014-0253-z

The Possible Association between Exposure to Air Pollution and Adverse Pregnancy Outcomes

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2011–2014

Objectives: To evaluate the possible association between exposure to air pollution during pregnancy and adverse birth outcomes among children born following assisted reproductive technology (ART) and spontaneously conceived (SC) pregnancies.

Methods: A historical cohort study comprising of 207,825 SC births and 8,905 ART births in Israel during the period 1997-2004 was used. Air pollution data were obtained from air monitoring stations and included SO_2, PM_{10}, NO_x and O_3. Geographic Information System (GIS) and kriging procedures were used to assess exposures during pregnancy. Logistic and Cox proportional hazards regression models were used to calculate the adjusted risk for adverse pregnancy outcomes including congenital malformations (CM), small for gestational age (SGA), low birth weight (LBW) and preterm birth (PTB). In addition, Air-Quality-Indexes (AQIs) for adverse birth outcomes were calculated.

Results: Higher levels of SO_2 exposure were not associated with an increased risk of any of the adverse outcomes. Increased levels of PM_{10} exposure were associated with an increased risk for CM and PTB, OR 1.06 (95%CI, 1.01-1.11) and OR 1.05 (95%CI, 1.02-1.08) per 10μg/m^3, respectively. Higher levels of NO_x exposure were associated with increased risk of CM and PTB, OR 1.03 (95%CI, 1.01-1.04) and OR 1.02 (95%CI, 1.01-1.04) per 10ppb increase respectively. Higher levels of O_3 exposure were associated with an increased, risk for SGA, OR 1.03 (95%CI, 0.99-1.08) and for LBW, OR 1.10 (95%CI, 1.02-1.18) per 10ppb increase. In the ART group higher levels of SO_2 were associated with slightly higher risk for CM and PTB and higher levels of O_3 exposure were associated with a slightly higher risk for all adverse outcomes. The feasibility, under certain assumptions, of creating an AQI for adverse birth outcomes has been demonstrated. Average air concentrations of different pollutants in an Israeli town were analyzed, yielding possible adverse birth outcomes as a function of 10μg/m^3 increases, PM_{10}, and to a lesser extent, NO_x.

Conclusion: Our initial results suggest that exposure to higher levels of air pollution during pregnancy may be associated with various adverse pregnancy outcomes. Although not significant, suggestion of higher impact of air pollution in the ART pregnancies was observed particularly for O_3 exposure. Further studies are warranted, including more accurate exposure data and a larger sample size for ART pregnancies to confirm these associations.

Research publications

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Impact of Exposure to Brominated Flame Retardants (BFRs) and Phthalates on Birth Outcomes in an Israeli Cohort

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2012–

Hypothesis: (1) Israeli pregnant women and their infants are widely exposed to brominated flame retardants (BFRs) and phthalates. (2) Exposure to these compounds is associated with adverse birth outcomes.

Background: BFRs and phthalates are used in many household and personal care products.

Objectives: (1) To assess BFRs and phthalates body burdens through measurement of these chemicals in maternal serum, urine and cord blood among several representative sub-populations. (2) To examine associations between exposure to BFRs and phthalates and (a) pregnancy complications, (b) anthropometrics at birth, (c) genital malformations and (d) maternal and infant thyroid function, sex steroids and corticosteroids. (3) To establish a bio-repository of these and other media (meconium, breast milk, father blood and urine) for future studies and to establish follow up methods for this cohort to later assess development and growth.

Justification: There are no published data on population exposure to BFRs in Israel. Data on phthalate exposure in Israeli pregnant women is limited. More data are required to characterize the health effects of these chemicals among pregnant women and children.

Experimental Methodology: 500 mother-child pairs will be recruited in Assaf Harofeh and Sourasky Medical Centers representing all sub-populations in Israel. Maternal blood and cord blood samples will be analyzed for BFRs and maternal urine samples will be analyzed for phthalates. Mothers will fill out a standardized questionnaire regarding life style factors, demographic information, and use of BFR and phthalate containing products. Anthropometrics will be recorded. Maternal and infant thyroid function, sex steroids and corticosteroids will be measured. The chemical analysis will be performed at the National Residue Control Laboratory. Quality control will be done with an international laboratory.

Expected contribution to environmental health in Israel: This study will provide important information on exposure during pregnancy, and will provide insights into the bioaccumulative nature of these chemicals. Such novel knowledge might provide insight regarding exposure sources unique to the Israeli general population and to sub-populations. This knowledge is essential for the general public, health professionals, scientists and policy/law regulators to base their understandings and recommendations for the future. This study will add to the growing body of international literature on exposure and health effects of environmental contaminants.

The Exposure of Pregnant Women and their Offspring to Endocrine Disrupting Chemicals and Organophosphate Pesticides

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2012–

There is a growing concern of the possible health effects posed by exposure to environmental contaminants. Of specific concern are vulnerable populations such as pregnant women and their developing fetuses. Phthalates, which are widely used in industry, are considered to be endocrine disrupting chemicals (EDCs), with a possible anti-androgenic effect. Organophosphate pesticides (OP) are widely used in agriculture and gardening; but while their possible effects in terms of carcinogenesis and neurologic disturbances have been widely studied, only few studies looked into the association of exposure with birth outcomes. Data are therefore lacking on the effects of phthalates and OPs on the developing fetuses, and there are no such data from Israel.

Our main objectives are to estimate intrauterine exposure to phthalates and OPs in the Jerusalem population, and to estimate the association of such exposures with birth outcomes and anthropometric features of the reproductive system. Our secondary objectives are to estimate the sources of exposure and the correlation between levels of these materials in amniotic fluid, maternal urine, and fetal urine collected soon after birth, in order to evaluate the validity of urine tests in estimating intrauterine exposure.

We are conducting a cohort study of women in their first trimester or early second trimester of pregnancy. Ongoing data collection started in September 2012. Data collection includes an interview and maternal urine sample upon recruitment, amniotic fluid and a second urine sample during follow-up visits in the second trimester, postpartum interview, examination of the offspring including anthropometric measurements of the anogenital distance (AGD), and a neonatal urine sample. All samples are kept in -80°c until shipment to the Friedrich Alexander University in Germany, for laboratory analysis.

As of May 2014, about 290 pregnant women have been recruited, of whom 93% were eligible for follow up and 164 have reached term. Of the 132 births that were identified at Hadassah, 102 neonates were examined by the study's neonatologists. In July 2014, 175 specimens from 73 women and their offspring were shipped for laboratory analysis.

Leveraging Telemedicine to Assess Associations between Acute Cardiovascular Events and Ambient Particulate Air Pollution in the Tel Aviv and Haifa Metropolitan Areas

Ronit Nirel[1] | Alon Peretz[2]
Uri Dayan[1] | Sara D. Adar[3]

1. The Hebrew University of Jerusalem
2. Rabin Medical Center
3. University of Michigan, USA

2012–

Research problem: Particulate matter (PM) air pollution in Israel is a major concern. Annual mean concentrations of PM in the Tel Aviv and Haifa areas are higher than in larger European cities. Cardiovascular morbidity is common in Israel. In 2009 there were more than 70,000 cardiac-related visits to the emergency room of subjects over 45 years old. Numerous studies have pointed to adverse cardiovascular effects due to PM air pollution, indicating a causal relationship between PM exposure and cardiovascular morbidity. It has been shown that the acute event onset time is essential for risk estimation, though this information is not yet broadly available. So far, there is only scarce scientific data regarding this association in Israel.

Objectives: To utilize a large and internationally unique telemedicine dataset in order to characterize the short term effects of PM on the cardiovascular system in two large Israeli cities. We also expect to better characterize the critical window of exposure to the incident cardiac events and subclinical changes, and explore how different weather conditions impact the intensity of the relationships with PM.

Expected contribution to environment and health: The proposed research will help to better understand the impacts of PM on cardiovascular disease on Israelis, for the first time. By leveraging a telemedicine service, this work will elucidate the critical timing of exposure to PM. Our work will identify sub-populations at increased risk and weather events that confer additional risk. This will help target prevention programs, create guidelines for susceptible individuals, and create efficient policies for managing air quality.

Methods: The study population is comprised of telemedicine subscribers living in the Tel Aviv and Haifa areas who called in relation to a cardiac event between 2002 and 2013. Cardiac events include phone calls for cardiac-related symptoms. Exposure to PM is assessed for time periods ranging from a half-hour to several days prior to the time of event. This study is a case-crossover design with time-stratified referent selection. Distinct weather conditions are explored as effect modifiers. We also explore relationships between air pollution levels and subclinical endpoints such as arrhythmias using mixed effects models.

Quantitative Evaluation of Organophosphate Pesticides and their Metabolites on Edible Crops

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Julius Ben-Ari[1]
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Dana Boyd Barr[3]

1. The Hebrew University of Jerusalem
2. Israel Ministry of Health
3. Emory University, USA

2013–2014

Our hypothesis is that exposure to organophosphate (OP) pesticides based solely on dialkyl phosphates (DAPs) urinary concentrations might lead to overestimation of the actual exposure to the parent OP pesticides. DAPs are present on sprayed crops and thus the measurement of urinary DAP concentrations reflect both direct exposure to the pesticides and also exposure to the metabolites. The objective of this study is to quantify OPs and DAPs in edible crops. This will enable us to estimate exposure to OP pesticides that take into account both exposures to the parent compound and to their metabolites. Detection of the specific metabolites will serve as an indicator of the preformation of the metabolites on the crops. Data from the Ministry of Agriculture and Rural Development shows that the produce most highly sprayed with OP pesticides is also highly consumed - apples, grapes, citrus fruits, tomatoes and cucumbers. Fresh samples will be analyzed.

Lung-on-Chip Alveolar Models for Inhaled Particle Cytotoxicity in Alveolar Epithelial Cells

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Peter Ertl[3]

1. Technion - Israel Institute of Technology
2. University of Fribourg, Switzerland
3. Austrian Institute of Technology, Austria

2013–2014

The fate of environmentally- or occupationally-inhaled ultrafine particles (UFPs), with diameters less than 100 nm, is drawing considerable attention due to potential health threats that emanate from human-related industrial activities. UFPs are now known to bypass the lung's defense mechanisms and penetrate across alveolar tissue, ultimately translocating into the systemic circulation. Epidemiological studies give evidence that high concentrations of UFPs, formed by gas-to-particle conversion and incomplete fuel combustion, may cause increased morbidity and mortality. Current nanotoxicology approaches to investigate inhaled UFP cytotoxicity in the lungs are still limited and often rely on UFP exposure over simple cell cultures. We are currently designing microfluidic lab-on-chip models of the alveolated airways of the lungs in an effort to develop an in vitro UFP exposure system of aerosol deposition on alveolar epithelial cells (AECs). Our efforts aim at designing novel approaches towards modern cytotoxicity assays of inhaled toxic UFPs that bypass animal models.

Research publications

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(2) Mahto, S.K., Charwat, V., Ertl, P., Rothen-Rutishauser, B., Rhee, S.W., & Sznitman, J. (2014). Microfluidic platforms for advanced risk assessments of nanomaterials. *Nanotoxicology, 22*, 1-15. Advance online publication. doi:10.3109/17435390.2014.940402

(3) Mahto, S.K., Tenenbaum-Katan, J., Greenblum, A., Rothen-Rutishauser, B., & Sznitman, J. (2014). Microfluidic shear stress-regulated surfactant secretion in alveolar epithelial type II cells in vitro. *American Journal of Physiology Lung Cellular and Molecular Biology, 306*, L672-L683.

(4) Tenenbaum-Katan, J., Fishler, R., Rothen-Rutishauser, B., & Sznitman, J. (2015). Microfluidic in vitro platforms of pulmonary alveolar physiology. *In IFMBE Proceedings 6th European Conference of the International Federation for Medical and Biological Engineering, Vol. 45*, 777-780. Advance online publication. doi:10.1007/978-3-319-11128-5_193

Endocrine Disrupting Chemical Burden among Residents of a Vegan-Organic Rural Community: The Amirim Study

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Thomas Göen[3]

1. Tel-Aviv Sourasky Medical Center
2. Israel Ministry of Health
3. Erlangen-Nuremberg University, Germany

2013–

Endocrine disrupting chemicals (EDCs) are suspected to be involved in diseases whose incidence has risen in the last decades such as obesity, diabetes, reproductive abnormalities, and endocrine-related cancers. Biomonitoring surveys of those EDCs in populations have pointed to geographical variations, possibly linked to lifestyle differences. The recent Israeli biomonitoring survey uncovered high levels of exposure of the Israeli population to BPA and phthalates when compared to the data available for the US and Canada. We hypothesized that, compared to the background omnivorous Israeli population, a lower burden of EDCs would be found among residents of the Amirim vegetarian/vegan village in the upper Galilee. The sample collection part of the study has now been completed and the mass spectrometry-based analytical part is underway. The results will be compared to those of the Israeli survey, and correlated to the anthropometric data and the numerous lifestyle and nutritional parameters we obtained. If the results confirm our hypothesis, this study will lay the ground for a long term life style intervention study.

Evaluation of Adverse Health Effects in the Israeli Population from Lack of Magnesium and Iodine in Drinking Water from Desalinized Sea Water

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Meital Shlezinger[1,2]
Michael Shechter[2]
Maya Leventer-Roberts[3]

1. Bar-Ilan University
2. The Chaim Sheba Medical Center at Tel Hashomer
3. Clalit Health Services

2014–

Extensive seawater desalination in Israel may decrease magnesium in drinking water (DW), causing hypomagnesemia and adverse health effects. We will study the association between consumption of desalinated drinking water (DSW) and serum magnesium in acute myocardial infarction (AMI) patients, the incidence of diabetes, hypertension and colorectal cancer. The study's specific components include: (1) Data on 11,683 AMI patients from the Acute Coronary Syndrome Israeli Survey (ACSIS) multi-center study (2002-2013): serum magnesium and clinical outcomes, controlled for risk factors; (2) Trends in serum magnesium in Clalit Health Services patients in regions with or without DSW, incidence of CV diseases, diabetes, colorectal cancer and hypothyroidism; (3) Association between serum magnesium and clinical outcomes in patients with AMI with a 1 year follow-up in 300 patients in regions supplied with DSW (Sheba MC) and 150 patients in regions with non-desalinated DW (Nahariya MC). (5) Urinary iodine in 150 pregnant women residing in areas with or without DSW, and neonatal thyroid functions. Potential positive findings may bear important consequences for public health in Israel.

Mortality Related to Traffic Air Pollution in a Vulnerable Population: A Contemporary Experience with a Novel Exposure Model

Yariv Gerber[1] | David Broday[2]
David M. Steinberg[1]

1. Tel Aviv University
2. Technion - Israel Institute of Technology

2014–

Misclassification bias due to imprecise exposure assessment is a major concern in the contemporary literature on air pollution's health effects. Using the ordinary kriging interpolation method, we previously were able to demonstrate, in a cohort of incident myocardial infarction (MI) patients, an association between chronic exposure to particulate matter at the participant's residence and several clinical outcomes during long-term follow-up. Yet, the approach to exposure assessment has relied on air-quality monitoring station records, resulting in incomplete temporal and spatial coverage. Recently, we have developed a novel model of exposure to traffic-related air pollution which incorporates dispersion properties and enables a spatially detailed estimation of air pollutants with a high temporal resolution. The present proposal aims to evaluate the association with long-term outcome and the discriminatory power of the newly developed exposure model in a geographically defined cohort (n=1,191) of patients with a history of MI followed up longitudinally. If proven suitable for epidemiological studies, this model could be applied to other settings and different populations.

Establishing a Station to Evaluate and Enhance Satellite-Based Estimates of Ground-Level $PM_{2.5}$ Levels for Health Applications in Israel

Yinon Rudich[1] | Ilan Koren[1]

1. Weizmann Institute of Science

2014–

Suspended particulate matter less than 2.5μm ($PM_{2.5}$) is an indicator of mortality and adverse health effects due to exposure to air pollution. Long-term exposure to $PM_{2.5}$ leads to increased mortality and morbidity from chronic cardiovascular and respiratory diseases, lung cancer, diabetes, and adverse birth outcomes. It was recently estimated that in 2010, outdoor $PM_{2.5}$ caused 3.2±0.4 million deaths and 76 million years of lost healthy life on a global scale. Given the implications and uncertainties of this estimate, it is imperative to improve estimates of $PM_{2.5}$ exposure. This proposal has two objectives: 1) to establish a SPARTAN validation site at the Weizmann Institute as part of a global network that will create a long term data set of $PM_{2.5}$ levels and composition; and 2) to evaluate and enhance remote sensing estimates of ground-level $PM_{2.5}$ in Israel's populated areas. The data from this site will be freely available for all researchers that conduct exposure studies in Israel.

Distributed Low Cost Mobile and Wireless Sensor Network for Air Quality Monitoring with Applications to Traffic Related Urban Air Pollution

David Broday[1]

1. Technion - Israel Institute of Technology

2010–2012

Development and application of sensor networks are currently an active research area due to their immense potential as personal monitoring devices. The project's goals were to examine the use of sensor networks for monitoring traffic related urban air quality. To accomplish this, we deployed a small (5 nodes) sensor network and tested its performance and limitations at the individual node and the network levels. We found that the sensors are seriously constrained by their power supply and that unlike stationary measurement sensor node mobility increased the complexity of data collection and analysis (e.g. GPS location recording depleted the node batteries very fast). Sensor measurements were compared against standard air quality monitoring data as well as against data from neighboring nodes, to examine the measurements accuracy and repeatability. The temporal, spatial, inter-nodal and inter-pollutant behavior of the sensors was as expected according to theoretical considerations. Whereas sensor performance was promising, lack of sensitivity, drift and interference of varying environmental stressors need careful consideration.

Phthalate Concentration in Child Use and Care Articles: Preliminary Screening of the Israeli Market

Jenny Gun[1] | Ovadia Lev[1]

1. The Hebrew University of Jerusalem

2010–2011

Numerous toxicological studies have proven the harmful influence of phthalates and their role as endocrine disrupting compounds in humans and mammals. Having in mind the dangerous influence of phthalate consumption even at trace levels, European directive 2005/84/EC restricted the content of six phthalates in toys and childcare articles. The aim of this research was to develop the analytical tools for the detection of banned phthalates in plastics and to provide the results of a preliminary analytical screening of the Israeli market in terms of the possible health risk. The preliminary analytical screening of the Israeli market revealed that a high percentage of the toys did not comply with European Directive and contained very high concentrations of the banned plasticizers. After receiving the results of the preliminary Israeli market screening of phthalate concentrations in toys, the Commissioner of Standardization of Israel turned to the Standards Institution of Israel (SII) to request a change in the standard for toys and childcare articles that will require limited concentrations of phthalates in this group of products.

Biological Monitoring of Ultrafine Particles in the Airways of Asthmatic Children

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Elizabeth Fireman[1]

1. Tel-Aviv Sourasky Medical Center

2012–2013

Exposure to air pollution triggers and exacerbates airway inflammation. Particulate material (PM) in ambient air pollution is characterized by aerodynamic diameter as being coarse (PM_{10}, range 2.5-10μm), fine ($PM_{2.5}$, range 0.1-2.5μm) and ultrafine (ultrafine particles [UFP] <0.1 μm). Animal studies have shown that inhaled UFP produce more inflammation than larger inhaled particles. Most of our knowledge on human exposure to PM is based on environmental monitoring. Our objective was to evaluate the effect of individual exposure to UFP on respiratory symptoms, respiratory function and airway inflammation in children aged 6-18 years who were referred to the Pulmonary and Allergic Diseases Department for evaluation due to respiratory symptoms. After obtaining consent, parents responded to a questionnaire on their child's symptoms. Spirometry, bronchial provocation challenge, induced sputum, and measurement of exhaled nitric oxide was performed. Exhaled breath condensate (EBC) was collected for analysis of UFP using the NanoSight Light Microscope LM20 by analyzing Brownian motion of the particle. Fifty-two children were included in the study. The total EBC particle count correlated with wheezing (R=0.28, p=0.04), breath symptom score (R=0.3, p=0.03), and sputum eosinophilia (R=0.64, p=0.005). The percent of EBC particles that were in the nano range size also correlated with wheezing (R=0.36, p=0.007), breath symptom score (R=0.33, p=0.02), and sputum eosinophilia (R=0.72, p=0.001). Nanoparticle exposure is correlated with respiratory symptoms and airway inflammation in children.

Exposure to Air Pollution and Long-Term Incidence of Frailty after Myocardial Infarction: A Pilot Study

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Vicki Myers[1]
Yaacov Drory (deceased)[1]

1. Tel Aviv University
2. Technion - Israel Institute of Technology

2012–2013

While exposure to air pollution has been associated with numerous health outcomes, the underlying pathways remain unclear. We evaluated the role of environmental exposures, including air pollution ($PM_{2.5}$) and neighbourhood socioeconomic context, in the development of frailty - a multidimensional age-related syndrome that indicates increasing vulnerability - in a cohort of first myocardial infarction (MI) survivors. Our results demonstrate a relationship between exposure to PM and frailty, providing a potential pathway with post-MI outcomes. The significant association suggests that chronic exposure to PM might affect multiple physiological systems in vulnerable MI patients, contributing to excess mortality not just through single processes, but by a broader assault on bodily systems. We further determined that frailer MI patients might be more sensitive to the adverse health effects of air pollution. These data provide evidence of the adverse health effects of chronic exposure to $PM_{2.5}$ among MI survivors residing in central Israel.

Research publications

(1) Myers, V., Broday, D.M., Steinberg, D.M., Yuval, Drory, Y., & Gerber, Y. (2013). Exposure to particulate air pollution and long-term incidence of frailty after myocardial infarction. *Annals of Epidemiology, 23*(7), 395-400.

(2) Gerber, Y., Myers, V., Broday, D.M., Steinberg, D.M., Yuval, Koton, S., et al. (2014). Frailty status modifies the association between air pollution and post-myocardial infarction mortality: A 20-year follow-up study. *Journal of the American College of Cardiology, 63*(16), 1698-1699.

(3) Myers, V., Drory, Y., Goldbourt, U., & Gerber, Y. (2014). Multilevel socioeconomic status and incidence of frailty post myocardial infarction. *International Journal of Cardiology, 170*(3), 338-343.

Assessment of Young Children's Exposure to Hazardous Chemicals Especially Neurotoxins, in Pre-Schools, Kindergartens and Homes in Northern Israel

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Yoram Finkelstein [2]
Igal Bar-Ilan[1]
Elyakim Doitsch[3]

1. Migal - Galilee Technology Center
2. Shaare Zedek Medical Center
3. Department of Education, Psychological Services, Hof Ashkelon Regional Council

2012

The pilot study assessed potential exposure to hazardous chemicals in rural and urban preschools and kindergartens in Israel. Eight facilities were inspected, tested for chemical residues, staff interviewed and parents surveyed. Pesticide was applied routinely in most facilities by licensed professionals or stored and applied illegally by facility staff. Children were exposed to herbicide Glyphosate (Roundup) and mosquito treatments. Indoor pesticide residues included developmental toxicants, suspected endocrine-disrupting chemicals and possible, likely and probable human carcinogens - all detected at very low concentrations. This could reflect heavy rains, gap since last pesticide application and delays in analyzing samples. Facility staff was mostly unaware of potential chemical hazards, guidelines for managing cleaning and disinfectant chemicals, or measures to reduce pest incidence. There are significant differences in building structure, chemical use and management between the US and Israel, and potential pesticides and chemical exposures. The study informed a larger survey and pilot intervention programs to reduce children's exposures in Israeli kindergartens and schools.

Environmental Health Policy: Inter-Agency Aspects at the Government Level

Maya Negev[1]

1. Tel Aviv University

2012–2014

In the government sphere, environmental health policy is inter-sectoral: the responsibilities are typically divided between the health agency and the environment agency. However, most of the decisions that impact environmental health are taken in agencies that are in charge of production, development and infrastructure. This study maps interagency dynamics concerning environmental health policy in the US as compared to Israel, and identifies the policy implications of different modes of collaboration. The mapping of mechanisms for interagency environmental health collaborations revealed a set of institutional, policy, research, and informal mechanisms. Following the mapping, two case studies of inter-sectoral collaboration in Israel were selected: regulation of pesticides in agriculture and the Clean Air Law. The mechanisms revealed were analyzed for strengths and weaknesses in both case studies. The study includes a set of recommendations for advancing environmental health policy in Israel.

The Association of Air Pollution and Blood Glucose Levels Among Patients with Diabetes in the Negev Region

Victor Novack[1] | Itai Kloog[2]
Idit F. Liberty[1]
Maayan Yitshak Sade[1, 2]

1. Soroka University Medical Center
2. Ben-Gurion University of the Negev

2013–

Studies suggest that diabetes mellitus is affected directly by air pollution, in addition to being an effect modifier for air pollution associated diseases. In turn, air pollution, which is known to increase inflammatory response, can induce insulin resistance and hyperglycemia. In this study, we aim to evaluate the temporal and spatial associations of particulate matter (PM_{10}, $PM_{2.5}$) and blood glucose (BG) level variations, among patients with diabetes in southern Israel. We retrieved daily data on air pollutants and meteorological variables for the period of 2001-2012 from the local monitoring station in Beer Sheva that records data every 20 minutes. Our preliminary results show significant increase of 0.44% (95%CI: 0.26%-0.59%) and 0.36% (95%CI: 0.24%-0.55%) in blood glucose, associated with an inter-quartile range increase in three day averaged SO_2 and NO_2, respectively. We are currently working on refining exposure estimates by using a novel satellite-based technique. With broad spatial coverage, satellites now allow us to predict daily PM levels at a 1x1 km spatial resolution, which greatly enhances our ability to estimate subject-specific exposures. These models allow for a better exposure assessment and thus reduce exposure error.

Monocytes and Macrophages as Integrators of Environmental Particles Exposure and Adipose-Derived Factors: Relevance to Adipose Inflammation in Obesity

Assaf Rudich[1] | Yinon Rudich[2]
James Schauer[3]

1. Ben-Gurion University of the Negev
2. Weizmann Institute of Science
3. University of Wisconsin-Madison, USA

2013–

Accumulating evidence supports a potential connection between environmental pollutants (EPs) and obesity and/or type-2-diabetes (T2DM). EPs constitute an independent predictor for T2DM, and obesity predisposes to deleterious metabolic effects of pollutants. We hypothesized a mediatory role for macrophages in EP's-induced adipocyte dysfunction. Macrophages were treated with water extracts of standard diesel engine particles with high/low content of organic compounds (SRM-1650/2975, respectively), and cultured adipocytes were then exposed to this conditioned-medium. SRM2975 increased dose-dependently the secretion of TNFα from macrophages, with no effect on IL-10. Furthermore, it attenuated adipocyte insulin signaling. These results support a biological path for obesity-induced sensitivity to the metabolic disrupting effects of EP exposure.

Estimating Intra-Urban Exposure Patterns to Traffic-Related Pollution with a Distributed Sensors Network

Ilan Levy[1] | David Broday[1]
Barak Fishbain[1]

1. Technion - Israel Institute of Technology

2012–

Research on the complex nature of air pollutants in populated areas is needed for obtaining a better understanding of exposure, source apportionment and representativeness of monitoring sites. Estimates of human exposure to air pollutants rely either on measurements taken by air quality monitoring sites, interpolation of measurements or model predictions. These methods, however, are unable to resolve the fine spatial structure of air pollutants concentrations in complex environments. This study aims to test the applicability of a novel and emerging technology for measuring air pollutants in an urban environment using a wireless distributed sensors network of small and affordable air pollution sensors. A network of several tens of stationary air quality nodes is deployed in Haifa, Israel. Each node is equipped with several pollution sensors (NO_2, O_3, CO and particles) as well as temperature, relative humidity, GPS and communication modules. Applying the network of tens of sensors over a period of few months will result in multiple samplings of each location, and allow a robust analysis.

Research publications

(1) Moltchanov, S., Levy, I., Etzion, Y., Lerner, U., Broday, D.M., & Fishbain, B. (2014). On the feasibility of measuring air pollution at dense urban areas by wireless distributed sensor networks. *Science of the Total Environment, 502*, 537–547. Advance online publication. doi: 10.1016/j.scitotenv.2014.09.059

Chemical Exposure, Granulosa Cell Exosomes, and Oocyte/Embryo Quality

Ronit Machtinger[1,2]
Andrea Baccarelli[3]
Russ Hauser[3]
Catherine Racowsky[3,4]

1. The Chaim Sheba Medical Center at Tel Hashomer
2. Tel Aviv University
3. Harvard University, USA
4. Brigham and Women's Hospital, USA

2013–

There is currently a concern regarding adverse effects from exposure to environmental chemicals that may act through disruption of the endocrine system (EDCs). In a recent in vitro study, we showed a dose-response association of bisphenol A (BPA) with the final stages of human oocyte maturation (Human Reproduction, October 2013). The mechanism(s) by which EDCs such as BPA and phthalates may affect oocyte maturation and embryo quality is not well understood. We hypothesize that exposure to BPA and phthalates impairs the signal transmission within the ovarian follicle. Novel studies have proposed that intracellular transmission of extracellular vesicles such as exosomes within the follicle might involve secretion and uptake of microRNAs (miRNAs). MiRNAs are short non-coding RNAs that target complementary mRNAs to silence their translation into proteins. Growing evidence indicates that exosome-contained miRNAs can transfer molecular signals among tissues through human fluids. The aims of this pilot study are to determine the associations of follicular fluid levels of BPA and phthalate metabolites among miRNA granulosa cell-derived exosomes with oocyte maturation and day three embryo quality.

Fellowships

Characterization of Urban to Neighborhood Scale Air Pollutant and Human Exposure using a Comprehensive Array of Fixed and Mobile Measurement Platforms

Fellow
Ilan Levy
Environment Canada

Supervisor
Jeffrey Brook

2008–2010

The complex behavior of primary and secondary air pollutants is a major challenge when evaluating human exposure to air pollution. While primary pollutants vary in time and space by the heterogeneity of emission sources, secondary pollutants also depend on the non-linear reactions between the former and both depend heavily on meteorology. Moreover, in order to fully understand the effect of the mix of pollutants on human health a better understanding of the multiple constituents and their interrelations is needed. These challenges require the use of multiple sources of information regarding the spatio-temporal variability of air pollutants, including a variety of measurement methods and models.

The Border Air Quality and Meteorology Study (BAQS-Met) field campaign examined the complexity of various processes influencing summertime ozone levels in the southern Great Lakes region of North America. Results from the field campaign were examined with respect to land-lake differences and local meteorology using a large array of ground-based measurements, aircraft data, and simulation results from a high resolution regional air quality model. Results show that the lakes act as a reservoir layer for ozone at night, which could cause elevated ozone levels over land during the day at the lake breeze flow.

The Montreal mobile lab measurements campaign in 2009 examined the feasibility of deploying a heavily instrumented mobile lab for characterizing air pollutants' spatial patterns and examined multi-pollutants' concentrations and interrelationships at the intra-urban scale. Comparison of the mobile lab averages to the adjacent air quality monitoring network stations to evaluate their representativeness showed that they were in reasonable agreement with the annual averages at the monitoring sites. This comparison provided some evidence that, through the deployment approach, the mobile lab is able to capture the main features of the average spatial patterns. The findings also indicate that the multi-pollutant mix varies considerably throughout the city, both in time and in space, therefore no single pollutant can be a perfect proxy measure for the entire mix under all circumstances. However, based on overall average spatial correlations with the suite of pollutants measured, nitrogen oxide species appeared to be the best available indicators of spatial variation in exposure to the outdoor urban air pollutant mixture.

Research publications

(1) Levy, I., Makar, P.A., Sills, D.M.L., Zhang, J., Hayden, K.L., Mihele, C., Narayan, J., Moran, M.D., Sjostedt, S., & Brook, J.R. (2010). Unraveling the complex local-scale flows influencing ozone patterns in the southern Great Lakes of North America. *Atmospheric Chemistry and Physics, 10*(22), 10895-10915.

(2) Makar, P.A., Zhang, J., Gong, W., Stroud, C., Sills, D.M.L., Hayden, K.L., Brook, J.R., Levy, I., Mihele, C., Moran, M.D., Tarasick, D.W., He, H., & Plummer, D. (2010). Mass tracking for chemical analysis: The causes of ozone formation in southern Ontario during BAQS-Met 2007. *Atmospheric Chemistry and Physics, 10*(22), 11151-11173.

(3) Sills, D.M.L., Brook, J.R., Levy, I., Makar, P.A., Zhang, J., & Taylor, P.A. (2011). Lake breezes in the southern Great Lakes region and their influence during BAQS-Met 2007. *Atmospheric Chemistry and Physics, 11*(15), 7955-7973.

(4) Dayan, U., Tubi, A., & Levy, I. (2012). On the importance of synoptic classification methods with respect to environmental phenomena. *International Journal of Climatology, 32*(5), 681-694.

(5) Levy, I. (2013). A national day with near zero emissions and its effect on primary and secondary pollutants. *Atmospheric Environment, 77*, 202–212.

(6) Levy, I., Mihele, C., Lu, G., Narayan, J., & Brook, J.R. (2014). Evaluating multipollutant exposure and urban air quality: Pollutant interrelationships, neighborhood variability, and nitrogen dioxide as a proxy pollutant. *Environmental Health Perspectives, 122*, 65-72.

(7) Levy, I., Mihele, C., Lu, G., Narayan, J., Hilker, N., & Brook, J.R. (2014). Elucidating multipollutant exposure across a complex metropolitan area by systematic deployment of a mobile laboratory. *Atmospheric Chemistry and Physics, 14*, 1-21.

Assessment of Dietary Exposure to Methylmercury and Polyunsaturated Fatty Acids through Fish Consumption and the Association with Cardiovascular Health

Fellow
Shirra Freeman
Harvard University, USA

Supervisor
James K. Hammitt

2009–2010

Fish are a source of high-quality protein, contain low levels of cholesterol and are one of few sources of polyunsaturated fatty acids (Omega-3) needed for neurodevelopmental, cardiovascular (CVD) and cognitive health. However, fish consumption may also increase the risk of exposure to a range of environmental toxins. Understanding and communicating the benefits and risks associated with eating fish is challenging and there is considerable confusion among the general public. In part, this is because most health advice targets women of childbearing age and young children with reference to the risks posed by methylmercury (MeHg) exposure for neurodevelopment. Dissemination of information on other health outcomes, environmental risks and nutritional benefits is much more limited.

The purpose of this research was to improve our understanding of the risks and benefits of fish consumption for cardiovascular health with reference to MeHg exposure and Omega-3 intake. NHANES data on US fish consumption, broken down by species was combined with US Department of Agriculture data on Omega-3 uptake and MeHg residues in fish tissue.The resulting exposure profile was used as a hypothetical dose and interpolated into dose-response functions from the literature using three different consumption scenarios: the national status quo based on the data; increasing consumption to 16oz per week in accordance with health recommendations (but without changing species mix); and changing species consumed.

Preliminary findings included: (1) the main source of MeHg exposure is tuna; (2) increasing fish consumption, without changing the mix of species leads to a proportionally larger rise in MeHg exposure than to Omega-3 uptake; (3) relatively small changes in the mix of species consumed, in particular lowering tuna and increasing shrimp and salmon consumption, improve the risk profile and do not entail significant additional cost; (4) a 15% reduction in MeHg exposure leads to an annual reduction of 151 CVD-related deaths.

The modeling platform developed in this research is currently being used as the basis for an Israeli case study. The platform has also been modified for use in a study of dietary pesticide uptake in a sample of Israeli children.

Particle Exposure Assessment

Fellow
Alexandra Chudnovsky
Harvard University, USA

Supervisor
Petros Koutrakis

2010–2012

The use of satellite data expands spatial coverage, enhancing our ability to estimate location- and/or subject-specific exposures to $PM_{2.5}$. The National Oceanic and Atmospheric Administration (NOAA) Geostationary Operational Environmental Satellite (GOES) has a long history of observations, thus its unique data is potentially extremely valuable for future epidemiological analyses. In our study we applied a daily calibration technique to aerosol optical depth (AOD) retrievals from the GOES Aerosol/Smoke Product (GASP) AOD data to predict $PM_{2.5}$ concentrations within the New England area of the United States. With this approach we could control for the inherent day-to-day variability in the AOD-$PM_{2.5}$ relationship, which depends on time-varying parameters such as particle optical properties, their vertical and diurnal concentration profiles and ground surface reflectance among others. The model-predicted values of $PM_{2.5}$ mass concentration were highly correlated with the actual observations, with a coefficient of determination of 0.89. Furthermore, based on the high quality predictions we investigated the spatial patterns of particle concentrations within the study area as they related to population and traffic densities.

In another study we reported on pollution spatial patterns derived from previously unavailable higher resolution (1km) Moderate Resolution Imaging Spectroradiometer (MODIS) AOD data. A new Multi-Angle Implementation of Atmospheric Correction (MAIAC) algorithm was developed for MODIS which provides AOD above bright urban areas at high spatial resolution. Using MAIAC data, the relationship between MAIAC AOD and $PM_{2.5}$ (as measured by the EPA ground monitoring stations) was investigated at varying spatial scales. Our analysis suggested that the correlation between $PM_{2.5}$ and AOD decreased significantly as AOD resolution degraded despite the intrinsic mismatch between $PM_{2.5}$ ground level measurements and AOD vertically integrated measurements. The fine resolution results indicated spatial variability in particle concentration at a sub-10 kilometer scale. This spatial variability of AOD within the urban domain was shown to depend on $PM_{2.5}$ levels and wind speed. Furthermore, this study was expanded and statistical models were developed to predict $PM_{2.5}$ concentrations. It was found that land use and meteorology impact pollution levels within the New England area.

Research publications

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Assessing Temporally-and Spatially-Resolved $PM_{2.5}$ Exposures for Epidemiological Studies Using Satellite Aerosol Optical Depth

Fellow

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Supervisor

Joel Schwartz

2010–2012

Accurate assessment of exposure to environmental pollutants is essential for establishing a relation between exposure to a certain pollutant and its health effects. During the past few years we have developed a novel method to quantitatively model the relationship between $PM_{2.5}$ measurements and MODIS satellite AOD (aerosol optical depth) across the North Eastern USA during the years 2000-2012. With broad spatial coverage, satellite data now allow us to expand exposure data well beyond ground monitoring networks into rural and suburban areas with spatial resolution down to 1 km, which greatly enhances our ability to estimate subject-specific exposures. Our models perform extremely well with an out-of-sample tenfold cross-validated R2 of 0.88. Importantly, these R2 values are for daily, rather than monthly or yearly values. We clearly demonstrated that using our prediction models reduces exposure error, resulting in better exposure assignment and also demonstrated how AOD can be reliably used to predict $PM_{2.5}$.

Using similar methodology we developed models to estimate daily air temperature from satellite surface temperature at a high spatial resolution of 1 km. Once again we demonstrated how satellite data can be used reliably to estimate daily air temperature at high resolution in large geographical areas.

These novel prediction models were later used in various health outcome studies. First, we used these daily $PM_{2.5}$ predictions to assign exposure to mortality cases in Massachusetts during the years 2000-2008. Then we used our prediction models for a study of the association between $PM_{2.5}$ exposure during pregnancy and reduced birth weight in Massachusetts during the years 2000-2008. We then studied the effects of short and long term $PM_{2.5}$ exposure on hospital admissions across New-England during the years 2000-2006 and across the Mid-Atlantic states between 2000-2008. In all the above studies we found a significant association between exposure to $PM_{2.5}$ and negative health effects.

Research publications

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(5) Kloog, I., Nordio, F., Coull, B.A., & Schwartz, J. (2012). Incorporating local land use regression and satellite aerosol optical depth in a hybrid model of spatiotemporal $PM_{2.5}$ exposures in the Mid-Atlantic states. *Environmental Science & Technology, 46*(21), 11913-11921.

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(8) Madrigano, J., Kloog, I., Goldberg, R., Coull, B.A., Mittleman, M.A., & Schwartz, J. (2013). Long-term exposure to $PM_{2.5}$ and incidence of acute myocardial infarction. *Environmental Health Perspectives, 121*(2), 192.

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(10) Chudnovsky, A.A., Koutrakis, P., Kloog, I., Melly, S., Nordio, F., Lyapustin, A., Wang, Y., & Schwartz, J. (2014). Fine particulate matter predictions using high resolution aerosol optical depth (AOD) retrievals. *Atmospheric Environment, 89*, 189-198.

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(12) Kloog, I., Nordio, F., Zanobetti, A., Coull, B.A., Koutrakis, P., & Schwartz, J.D. (2014). Short term effects of particle exposure on hospital admissions in the Mid-Atlantic states: A population estimate. *PloS ONE, 9*(2), e88578.

Molecular Epidemiology of Lung Function: An Integrated Approach

Fellow

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Supervisor

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2010–2012

Chronic obstructive pulmonary disease (COPD) poses a heavy morbidity and mortality burden on both individual patients and society. In its severe stages, it is associated with functional impairment, reduced quality of life, recurrent exacerbations, systemic manifestations and increased mortality risk. Recently, it has been established that once the disease has occurred, patients with COPD have increased levels of both airway and systemic inflammation and that the intensity of systemic inflammation correlates with the severity of the disease. However, it remains unknown whether levels of systemic inflammation can identify smokers at risk of COPD during their young to middle adult life, how inflammatory markers interact with molecules involved in other pathogenetic pathways, and whether integration of information from multiple biomarkers and from variation in their encoding genes can improve their predictive value on decline of lung function.

The project's main objective was to identify systemic biomarkers of decline of lung function using the Spanish branch of the prospective population-based European Community Respiratory Health Survey (ECRHS). We tested 20 biomarkers in serum, variably involved in inflammation, innate immunity, proteolysis, oxidative stress, auto-immune responses and other potential pathways. A large group of candidate genes related to the above biomarkers was also genotyped. A complete screening of all measured biomarkers against concomitant lung function levels has been completed. Screening of all genotyped single nucleotide polymorphisms (SNPs) against biomarkers levels resulted in multiple significant associations, suggesting that many of these proteins are under significant genetic control. The aim to determine whether the above associations are different in smokers as compared with non-smokers and in asthmatics versus non-asthmatics has been achieved. This was achieved by stratified analyses in which biomarkers were related to concomitant levels and subsequent decline of lung function in these different groups separately. With some notable exceptions, most associations did not differ across these groups. Large amounts of molecular data have been produced and will benefit future studies. For example, now that prospective data for the third survey are available, we hope temporal sequence between biomarkers and clinical phenotypes could be resolved and these data can be used to generate models of risk prediction.

Research publications

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The Effect of BPA on Human Oocyte Maturation – In Vitro Study

Fellow

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Supervisors

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2010–2012

The main focus of this research was to investigate the effect of the environmental chemical, bisphenol A (BPA) on normal human oocyte (egg) development. Potential sources of BPA exposure include drinking water, air and dust, as well as polycarbonate baby bottles, tableware, white dental fillings and sealants and the resin lining of cans used in food and beverage products. BPA was detected in human fluids such as urine, serum, fetal serum, amniotic fluid and follicular fluid, the fluid that embeds the oocyte.

Immature oocytes (GV) from patients undergoing IVF procedure, which would otherwise be discarded, were used following patient signed informed consent for donation of their discarded oocytes for research.

Oocytes from only one cycle of each patient were included in the study. A total of 352 oocytes were cultured with 0, 20, 200 ng/ml or 20 µg/ml of BPA. Oocytes were then fixed and labeled for tubulin, actin and chromatin and assessed with confocal microscopy for their meiotic stage. Mature oocytes (MII) (n=175) were further classified according to their spindle configurations and patterns of chromosome alignment.

We showed a decrease in the percentage of oocytes that normally developed (progressed to MII) as the BPA dose increased ($p=0.002$). As BPA dose increased, there was an increase in the percentage of oocytes that were degenerated ($p=0.01$) or that had undergone abnormal spontaneous activation ($p=0.007$). Among MII oocytes, as the BPA dose increased, there was a significant decrease in the incidence of bipolar spindles ($p<0.0001$) and aligned chromosomes ($p=0.02$).

Research publications

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Breast Cancer and Epigenetics

Fellow

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Supervisor

Mary Beth Terry

2011–2013

One plausible mechanism by which the environment can alter breast cancer susceptibility is through epigenetic effects on somatic cells, leading to activation or silencing of key genes in critical pathways. Epigenetic processes which include DNA methylation, altered packaging with histones and genomic imprinting and aberrations of these processes play a role in causing cancer. Accumulating data suggest not only that global DNA hypomethylation may be related to cancer but that environmental factors may alter DNA methylation patterns. In addition, there is evidence that environmental exposures associated with cancer risk are also associated with genomic DNA hypomethylation. While epigenetic modifications may occur at any age, they are more likely to occur early in embryonic or fetal development, during puberty, and in old age.

We are conducting a unique study on human exposure to organchlorines during pregnancy and the effect that these compounds may have on epigenetic events during two windows of exposure that are critical to the breast: (1) pregnancy, when ductal proliferation places the breast at risk for carcinogenesis in the mother and (2) the prenatal period when breast cellular differentiation places the breast at risk for carcinogenesis in the daughter. There are few human studies where exposure to endocrine active compounds during these critical periods can be measured directly in relation to subsequent breast cancer risk. The proposed research is a novel and unique opportunity to address this gap by efficiently using an existing cohort that spans two generations. This study uses a 50-year follow-up of the Child Health and Development Studies (CHDS) Pregnancy Cohort. The cohort includes maternal pregnancy serum samples that were collected during peak exposure to organochlorine pesticides and polychlorinated biphenyls in the 1960's, prior to the ban on these chemicals. DNA methylation in adulthood will be added as an outcome to the study of in utero organochlorine exposure and breast density (n=200). In addition we will examine whether prenatal organochlorine exposure is associated with DNA methylation measured using the adult sera of women.

A review article published as part of this study examined the differences in white blood cells DNA methylation by selected risk factors. The conclusions uniquely suggest that there are correlations between early life exposure to environmental factors and DNA methylation.

Research publications

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Traffic-Related Air Pollution and Noise and Blood Pressure of Children: Results from the PIAMA Birth Cohort Study

Fellow

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Supervisor

Bert Brunekreef

2012–2013

Very little is known about the effects of traffic-related air pollution (TRAP) on blood pressure (BP) in children. TRAP and noise share traffic as a common source, and both have been suggested to be positively associated with BP in adults. We investigated the associations of short- and long-term exposures to TRAP, as well as long-term exposure to traffic noise (TN) with BP in 12 year-old children from the PIAMA birth cohort study followed from pregnancy until the age 12.

TRAP concentrations at the participants home and school addresses during the time of BP measurements were estimated by land use regression (LUR) models. The models were based on TRAP monitoring campaigns performed between February 2009 and February 2010 which included measurements of nitrogen dioxide (NO_2), ''soot'' (determined as the reflectance of $PM_{2.5}$ filters), $PM_{2.5}$, and PM_{10}. The LUR models were used to estimate TRAP concentration at the participants' addresses, using the same GIS predictor variables. Daily data on NO_2, PM_{10} and ozone from routine background monitoring sites located in the study area were used to estimate short-term exposures. Road TN at the participants' home and school addresses at the time of BP measurements was estimated using the EMPARA noise mapping model for the Netherlands. We were able to geocode home addresses and assign TRAP and TN exposures for 1,400 of the 1,432 children with BP.

We observed that diastolic BP tended to increase with increasing long-term TRAP exposure at home and school addresses. The associations were stronger for children who lived at the same address since birth. The associations became slightly stronger for NO_2, $PM_{2.5}$ absorbance and $PM_{2.5}$ after exclusion of children with doctor-diagnosed asthma and/or diabetes.

In addition we investigated the association between particulate matter composition and BP. Annual average concentrations of copper, iron, potassium, nickel, sulfur, silicon, vanadium, and zinc in particles with diameters of less than 10μm (PM_{10}) and 2.5μm ($PM_{2.5}$) were estimated. We found a positive association between diastolic BP and iron, silicon, and potassium in PM_{10} and between iron and silicon in $PM_{2.5}$. The association with iron may indicate the health relevance of non-exhaust emissions from traffic.

Research publications

(1) Bilenko, N., Rossem, L.V., Brunekreef, B., Beelen, R., Eeftens, M., Hoek, G., Houthuijs, D., de Jongste, J.C., Kempen, E.V., Koppelman, G.H., Meliefste, K., Oldenwening, M., Smit, H.A., Wijga, A.H., & Gehring, U. (2013). Traffic-related air pollution and noise and children's blood pressure: Results from the PIAMA birth cohort study. *Journal of Preventive Cardiology*. Advance online publication. doi: 10.1177/2047487313505821

In Utero and Early Childhood Pesticide Exposure and Respiratory Symptoms and Lung Function in Children

Fellow

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Supervisor

Brenda Eskenazi

2012–2014

The causes of chronic respiratory disease are not fully understood. Exposure to environmental pollutants such as air pollution has been linked to chronic pediatric respiratory disease. Although pesticide use is widespread and known to have potential adverse health effects, the contribution of organophosphate pesticides (OPs) to the development of these disorders is not well described. OPs can affect respiratory function by inhibition of acetylcholinesterase. Additionally, recent reports from animal studies show that at doses below those that can cause acetylcholinesterase inhibition, OPs can induce airway hyper-reactivity. This is potentially important for the occurrence and severity of respiratory chronic disease.

The project's main objective was studying the association between prenatal and early childhood exposure to OPs and respiratory symptoms and spirometry measures in the CHAMACOS (The Center for the Health Assessment of Mothers and Children of Salinas) prospective birth cohort. The CHAMACOS center is aimed at studying the association between exposure to pesticides and other environmental agents and the health of pregnant women and their children. The study followed 526 pregnant women to delivery of a live-born, surviving singleton. Mothers were interviewed twice during pregnancy, after delivery, and six times during childhood. Dialkyl phosphate (DAP) metabolites of OPs were measured in urine samples from mothers, twice during pregnancy, and in urine samples from their children, five times during childhood.

The results show that higher prenatal DAP metabolite concentrations in urine were associated with increased odds of respiratory symptoms consistent with possible asthma in the children five to seven years later. Additionally, childhood exposure assessed by DAPs was also associated with respiratory symptoms at ages five and seven and with pulmonary lung function measurements in 7-year-old children.

This is the first report on adverse associations between early-life OP exposure and respiratory symptoms and spirometry measurements in children. The strengths of the study include a prospective design, use of biomarkers for exposure assessment instead of relying on questionnaire data, and use of the objective measurement of spirometry tests in addition to symptoms reports.

Research publications

(1) Raanan, R., Harley, K.G., Balmes, J.R., Bradman, A., Lipsett, M., & Eskenazi, B. (2014). Early-life exposure to organophosphate pesticides and pediatric respiratory symptoms in the CHAMACOS cohort. *Environmental Health Perspectives*. Advance online publication. doi: 10.1289/ehp.1408235

Association between Air Pollution and Incidence of Autism Spectrum Disorder in the Nurses' Health Study II

Fellow
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Supervisor
Marc Weisskopf

2012–2014

Autism spectrum disorder (ASD) is a developmental disorder with increasing incidence worldwide, yet with unclear etiology. Recent studies suggest that environmental factors in fetal development are part of the etiology. The Nurses' Health Study II (NHS II) is a large cohort of female nurses in the United States that have been followed with biennial questionnaires since 1989. The autism project in NHS II includes participants from across the US, and utilizes a nested case control approach, eliminating many of the potential biases associated with comparisons in previous studies.

The aim of the current project is to explore the association between maternal exposure to particulate matter (PM) air pollution and risk of ASD. Mother's address at birth was geocoded and linked to ambient $PM_{10-2.5}$ and $PM_{2.5}$ estimates, using the generalized additive models of these pollutants for the continental US. These models use ambient PM data from air quality and research monitoring networks, meteorological variables from weather databases and site characteristics from GIS. Average exposure measures were calculated for the period the mother was pregnant with a case or control child in the sample, and for adjacent 9-months periods. Subjects were NHS II participants' children born between 1990-2002 with ASD (n=245) and without ASD (n=1,522). Participants were randomly selected using frequency matching for birth years and ASD diagnosis was based on validated maternal report.

We found that $PM_{2.5}$ exposure during pregnancy was associated with increased odds of ASD, with the 4th exposure quartile having an adjusted odds ratio (OR) of 1.71 (95% CI: 1.10, 2.66) compared with the 1st quartile. The association was stronger when limiting the sample to those who did not change residences around the time of pregnancy (OR=2.02, 95% CI: 1.15, 3.54). ASD associations with $PM_{2.5}$ exposure nine months before or after the pregnancy were substantially lower. During pregnancy, $PM_{2.5}$ exposure during the third trimester had the strongest association (OR=1.49 per inter-quartile range increase in $PM_{2.5}$ [4.40 $\mu g/m^3$], 95% CI: 1.20, 1.85) with ASD. There was no association between $PM_{10-2.5}$ and ASD. In conclusion, higher exposure to $PM_{2.5}$ during pregnancy, and especially during the third trimester, is associated with risk of ASD.

Research publications

(1) Raz, R., Weisskopf, M.G., Davidovitch, M., Pinto, O., & Levine, H. (2014). Differences in Autism Spectrum Disorders incidence by sub-populations in Israel 1992–2009: A total population study. *Journal of Autism and Developmental Disorders*. Advance online publication. doi:10.1007/s10803-014-2262-z

Birth and Childhood Weight and Environmental Exposures

Fellow

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Supervisors

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2013–2014

Child weight status is an important health outcome. The aim of the study was to evaluate the effect of exposures to the environment during pregnancy and child weight status in Israel and in Spain. We evaluated the associations between the built environment and birth weight in an Israeli registry based cohort. Evaluation of the associations between proximity to green spaces and surrounding greenness and birth weight for approximately 40,000 singleton live births in Tel-Aviv was performed. Satellite-based Normalized Difference Vegetation Index and proximity to major green spaces from OpenStreetMap were used. We observed that an increase in one interquartile range greenness was associated with a statistically significant increase in birth weight (19.2g, 95% CI: 13.3 to 25.1) and decreased risk of low birth weight cases (OR=0.84, 95% CI: 0.78 to 0.90). The findings were consistent with different buffer and green space sizes and stronger associations were observed among cases of lower socioeconomic status.

In the Spanish INMA (Infancia y Medio-Ambiente) birth cohort we evaluated the effects of maternal exposure to multiple chemicals on child weight status at age seven. We evaluated associations between pre- and perinatal biomarker concentrations of 27 endocrine-disrupting chemicals (EDCs) and child weight status in 470 children aged seven, using single and multi-pollutant models. The 27 EDCs measured include: ten phthalate metabolites, bisphenol A, cadmium, arsenic, and lead in two maternal pregnancy urine samples, six organochlorine compounds in maternal pregnancy serum, mercury in cord blood, and six polybrominated diphenyl ether congeners in maternal colostrum. Principal component analysis generated four factors that accounted for 43.4% of the total variance.

The organochlorine factor was associated with child weight status and an increased risk for overweight (adj RRs tertile 3 vs 1: 2.59, 95% CI: 1.19, 5.63) and this association was robust to adjustment for other EDCs. Children located in the second tertile of phthalates factor exposure had inverse associations. This study suggests that prenatal exposure to organochlorines is associated with increased risk of overweight in children and that exposure to other EDCs does not confound this association. This work demonstrated the importance prenatal exposures have on children's weight status.

Research publications

(1) Agay-Shay, K., Peled, A., Crespo, A.V., Peretz, C., Amitai, Y., Linn, S., Friger, M., & Nieuwenhuijsen, M.J. (2014). Green spaces and adverse pregnancy outcomes. *Occupational and Environmental Medicine, 71*(8), 527-528.

Traffic Related Air Pollution and Acute Health Response – Evidence from Panel-Based Studies

Fellow
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Supervisor
Jeremy Sarnat

2013–2015

Considerable evidence from observational and controlled studies link traffic-related pollution to adverse health effects. The identification of specific emission sources, components and mixtures of traffic pollution associated with acute and chronic response remains a key knowledge gap within air pollution health effects research.

The Atlanta Commuters Exposure studies (ACE-1 and ACE-2)

To investigate in-vehicle exposures among daily car commuters, we conducted ACE-1 and ACE-2; two panel-based exposure and health assessment studies among adults with and without asthma. In ACE-2, a randomized, crossover study, 60 adults participated in a scripted two hour highway commute in addition to either a surface street commute or an indoor clinic exposure scenario. Each scenario included an extensive suite of pre- and post-exposure pollutant and health measurements. ACE-2 is part of a larger USEPA-supported initiative, the Southeastern Center for Air Pollution and Epidemiology, designed to examine health effects associated with air pollution mixtures. Specifically, ACE-2 aims include examination of:

- acute, sub-clinical oxidative stress-mediated responses due to real-world exposures to traffic-related PM, using individual-specific metrics of personal exposure;
- the temporality of these exposure-response functions;
- whether daily commuters comprise a potentially vulnerable sub-population; and
- whether asthma status and control modifies the risk of traffic PM.

Developing Multi-pollutant Exposure Indicators of Traffic Pollution: The Dorm Room Inhalation to Vehicle Emissions (DRIVE) Study

DRIVE is a field-based measurement and exposure study, which will evaluate a suite of primary traffic pollution indicators and novel biomarkers of internal pollutant exposures using environmental metabolomics. The DRIVE study focuses on a unique emission-exposure setting in Atlanta. The Georgia Institute of Technology students live in residential dorms immediately adjacent to the busiest and most congested highway artery in the city. Sixty students living in these dorms will be recruited for the collection of time-activity information and measurement of metabolic biomarkers of exposure. In this study we will conduct highly chemically-speciated measurements of traffic pollutants in a range of near road microenvironments and assess the suitability of using near road indicators as primary traffic exposure surrogates in panel-based and small cohort epidemiological studies. Metabolomics results may lead to the development of new biologically-based primary traffic pollution indicators.

Research publications

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Association of Long-Term Exposure to Air Pollution and Noise with Neurocognitive Functions in the Heinz Nixdorf Recall Study Cohort

Fellow

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Supervisor

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2013–2015

Investigations of the association between air pollution and ambient noise to neurocognitive function are scarce, mostly performed on children and adolescent populations, and the results are inconsistent. The effect of long-term air pollution and ambient noise exposures on cognitive functions and on Mild Cognitive Impairment (MCI) (the intermediate state between normal cognitive aging and dementia) in the adult population has not yet been investigated.

The post-doctoral project is performed on participants from the Heinz Nixdorf Recall Study (Risk factors, Evaluation of Coronary Calcium and Lifestyle), a population-based longitudinal study from three cities in the German Ruhr Area: Bochum, Essen and Mülheim/Ruhr. We estimated exposure to the air pollutants $PM_{2.5}$, PM_{10}, and NO_2 using two types of exposure models – European Air Pollution Dispersion and Chemistry Transport Model (EURAD-CTM), and land use regression ESCAPE-LUR. Long-term exposure to traffic noise was modeled as weighted 24-h mean (L_{DEN}) and weighted night-time mean (L_{NIGHT}) in dB(A). 4,814 randomly chosen participants (45-75 years of age) were enrolled into the study between December 2000 and August 2003. After five years (2006-2008) the first follow-up visit was performed, and it included a screening test of amnestic and cognitive functioning. Five tests were used to assess the cognitive status of participants: immediate and delayed word recall tests, clock drawing test, labyrinth test, and animal naming test. Results of each of these tests were normalized and adjusted for age and education status of participants based on age-specific norms of cognitive subtests for the German general population. A global cognitive score was calculated as a sum of normalized scores of performance for the five tests used for cognitive assessment. Of the 4086 participants that completed the cognitive tests, 579 were diagnosed with MCI (n=309 amnestic and n=283 non-amnestic MCI).

The aim of this study is to analyze the associations between long-term exposure to air pollution and ambient noise and the following outcomes: overall MCI, amnestic and non-amnestic MCI subtypes, each of the five cognitive tests independently, and with a global cognitive score. The analysis will be performed using cross-sectional and longitudinal study designs.

Research publications

(1) Tzivian, L., Winkler, A., Dlugaj, M., Schikowski, T., Vossoughi, M., Fuks, K., Weinmayr, G., & Hoffmann, B. (2014). Effect of long-term outdoor air pollution and noise on cognitive and psychological functions in adults. Review article. *International Journal of Hygiene and Environmental Health*. doi: 10.1016/j.ijheh.2014.08.002

The Polybrominated Biphenyl (PBB) Cohort

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2013–2015

Brominated flame retardants (BFRs) are synthetic chemicals, found in a wide variety of consumer products including fabrics, furniture, plastics, computers and other electronics. BFRs may be toxic and show hormonal or anti-hormonal properties in vitro and in wildlife. These chemicals have been associated with adverse health effects in humans, including spontaneous abortions and breast cancer. A unique opportunity to study possible effects of BFR exposure was presented in the mid 1970s, when Michigan residents, as a result of an industrial accident, were exposed to Polybrominated Biphenyl (PBB), a member of the BFR chemical group, through contaminated food. Prior to the Michigan disaster, little was known about the possible human health effects of BFRs. Early studies in exposed residents focused on acute health effects such as liver, immune, and neurological function. Later, as concern grew about the endocrine-disrupting potential of these chemicals, studies focused on reproductive effects. Because PBB can cross the placenta and concentrates in breast milk, children born after the incident were exposed in utero and early infancy, during a critical window in their development. Participants have been followed for 40 years and three generations, enabling, apart from direct exposure-outcome assessment, to study the possible fetal origins of adult disease and multigenerational effects of exposure, including biological mechanisms, epigenetic phenomena and gene-environment interactions. This cohort includes over 4,000 Michigan residents.

At this stage the focus is on recruiting study participants from the original PBB cohort, in order to engage them in ongoing studies. This involves having community meetings, working with participants to administer informed consent, complete questionnaires, facilitate specimen collection and anthropometric measurements. All participants are asked to provide a blood sample to measure current PBB blood levels.

These studies are assessing several health outcomes, and include three levels of participation. The first level involves completion of a general health questionnaire which includes questions on thyroid dysfunction, neurodegenerative and musculoskeletal disorders and cancer. In level two, participants in reproductive age groups are offered to participate in a reproductive health study, which includes: anthropometric body measurements, height, weight, body fat percentage and digits 2 and 4 ratio, and completing an in-depth questionnaire on reproductive history and gender-specific reproductive health dysfunction, cancers and treatments. The third, more detailed level of participation, involves collection of human specimen (semen and urine in males; three menstrual cycles daily urine in females), which will be analyzed for hormone levels and activity, menstrual function pattern, spermatogenesis and infertility.

Analysis of the data will clarify the possible association between level of exposure to PBB and the risk for selected, general and reproductive adverse health outcomes.

Male Fertility and Environmental Exposures

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Supervisor
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2014–

Male reproductive health and fertility is of considerable public health importance due to its high medical, societal and economic burden and use as a predictor of morbidity and mortality. In addition, male reproductive health and fertility is sensitive to the impacts of modern environment on human health, such as exposures to endocrine disrupting chemicals (i.e. pesticides) and could serve as a ''canary in a coal mine''. There is growing evidence that there may be a common environmental etiology for several male disorders such as reduced semen quality (SQ), cryptorchidism, hypospadias and testicular cancer.

The statements of Carlsen et al. in 1992 and Swan et al. in 2000 that SQ had declined over the past 50 years remain controversial. An evidence-based answer to this important question requires rigorous scientific effort that takes into account all new data published since 1996 and synthesizes it by proper analytical methods.

The aims of the current study will be to identify contemporary temporal trends and geographic variability in sperm concentration and examine modification of temporal trends by geographic location. We will conduct a systematic literature review and meta-analysis of all studies of semen quality in populations unselected by fertility status published since 1996. From each study, we will extract data on semen parameters, semen collection and analysis methods, temporal and spatial variables, study population, study variables and quality, and personal variables. We will use multiple complex analytical methods to model temporal changes. We will use stratified and meta-regression methods to examine geographic variability, controlling for covariates. Interactions between time and geographic region will be analyzed.

Metabolomics and Adductomics Analysis of Dried Blood Spots (DBS) from the Northern California Childhood Leukemia Study (NCCLS)

Fellow

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Supervisor

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2014–

Since 2001 researchers have mainly examined the human genome (G) to discover causes of disease despite evidence that G explains only 10-15% of the chronic-disease risks. Therefore, it is probable that most of these risks arise from the exposome (E, representing all exposures) and from G×E interactions. Since both endogenous and exogenous exposures express themselves chemically, blood specimens can be used for conducting exposome-wide association studies (EWAS) in order to identify causal environmental exposures. An EWAS begins by comparing profiles of thousands of small molecules (metabolomics) and/or large molecules (proteomics) in serum or plasma from diseased and healthy subjects. Omic features that differ between populations are then identified and used as targeted biomarkers in follow-up studies to confirm causality, to identify exposure sources, and to investigate mechanisms of action.

Leukemia makes up approximately 35% of all childhood cancers (ages 0-14), yet, its etiology is mostly unknown. Established risk factors (e.g. genetic conditions, ionizing radiation, and chemotherapeutic agents) account for only 10% of the causes, while suspected risk factors include chemical exposure, tobacco smoke, viral infection, dietary exposures, and non-ionizing radiation exposure of either the child and/or parent.

Using the EWAS approach, a subset of dried blood spots (DBS) from the Northern California Childhood Leukemia study (1,000 cases and controls) will be analyzed using mass-spectrometry-based metabolomics and adductomics (a variant of proteomics that focuses on adducts of reactions between human serum albumin and reactive electrophiles) to identify and quantify discriminating features between cases and controls. Using elements of exposure biology, the molecular linkages between exposure and disease risk will be explored. As the DBS were obtained prior to the onset of disease during routine heal prick after birth, this matrix offers a unique snapshot of prenatal exposure.

Congenital Malformations and Associations with Ambient Air Pollution in Israel, 2000-2006

Fellow
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University of Haifa

Supervisors
Shai Linn,
Amatzia Peled and
Chava Peretz

2008–2011

The main aim of our study was to evaluate the association between maternal exposures to air pollution and ambient temperature during pregnancy and congenital malformations (CM) risk in Israeli women. On the national level, ecological analyses for the total of 1,000,000 births (live births, stillbirths, late abortions and CM) were conducted. All maternal addresses were geocoded. Socio-demographic risk factors and non-random patterns in time and space were evaluated using Poisson trend harmonic method, LISA and SaTScan. The analyses were conducted for 45 CM sub-groups. In a retrospective cohort from the Tel Aviv area we analyzed the associations between CMs thought to be related to environmental factors, mainly congenital heart defects (CHD), and maternal exposure to ambient air pollution and ambient temperature during weeks 3-8 of pregnancy. We found that maternal exposure to increased concentrations of PM_{10} and ambient temperature during the winter was associated with increased risk for multiple CHD. Results for PM_{10} confirm results from previous studies. Results for ambient temperature are novel.

Research publications

(1) Agay-Shay, K., Friger, M., Linn, S., Peled, A., Amitai, Y., & Peretz, C. (2012). Periodicity and time trends in the prevalence of total births and conceptions with congenital malformations among Jews and Muslims in Israel, 1999-2006: A time series study of 823,966 births. *Birth Defects Research Part A: Clinical and Molecular Teratology, 94*(6), 438-448.

(2) Agay-Shay, K., Amitai, Y., Peretz, C., Linn, S., Friger, M., & Peled, A. (2013). Exploratory spatial data analysis of congenital malformations (CM) in Israel, 2000–2006. *ISPRS International Journal of Geo-Information, 2*(1), 237-255.

(3) Agay-Shay, K., Friger, M., Linn, S., Peled, A., Amitai, Y., & Peretz, C. (2013). Air pollution and congenital heart defects. *Environmental Research, 124*, 28-34.

(4) Agay-Shay, K., Friger, M., Linn, S., Peled, A., Amitai, Y., & Peretz, C. (2013). Ambient temperature and congenital heart defects. *Human Reproduction, 28*(8), 2289-2297.

Study of the Relationship between Spatial Dispersion of Ischemic Heart Diseases and Respiratory Diseases and Meteorological, Vehicular Air Pollution and Socio-Economic Factors in Israel's Negev Region

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Supervisors
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Michael Friger

2008–2011

The research focuses on the short term effects of meteorological, vehicular NO_x air pollution (VNAP) and socioeconomic (SES) factors on daily hospitalization rates of respiratory (RD) and ischemic heart diseases (IHD) in Beer Sheva during the years 2003-2007. While the association between meteorology and health effects has been extensively studied, findings regarding the relationship between VNAP exposure and health outcomes are still controversial and subject to debate. Our aim was to investigate the association between VNAP exposure, meteorological and SES factors and daily hospitalizations for IHD and RD. Significant spatio-temporal variations of NO_x were found within Beer Sheva. Vehicular NO_x was associated with daily hospitalizations for RD and IHD. Mean daily temperature and relative humidity were found to be associated with acute RD in the young age group (0-14) and chronic RD and IHD in the elderly (65+). SES was associated with daily hospitalizations by season for RD and IHD. The highest daily hospitalizations for all seasons were found in the lowest SES level for RD and in the medium SES level for IHD.

Multicultural Public Participation in Health Impact Assessment

Fellow
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2008–2011

Health impact assessment (HIA) was developed to systematically review plans, projects and policies and recommend alternatives which maximize health gains and minimize health inequalities. HIA includes stakeholder participation, in order to democratize decision-making and utilize knowledge, values and priorities of diverse populations. However, such participation is challenging and complex. The research aim was to suggest a model for multicultural stakeholder participation. As part of the research, stakeholder participation was included in the Beer Sheva metropolitan plan, focusing on land-uses in the vicinity of Ramat Hovav. A steering committee was established, and meetings, focus groups, interviews and observations conducted. The data were analyzed using qualitative methods. The research presents the manifestations of the multiplicity of sectors in HIA, and the challenges raised regarding knowledge, language and risk perception. In addition, the relationships between technical and local knowledge are explored. The research shows that technical knowledge may be disputable, uncertain and based on assumptions while local knowledge includes objective and systematic methods. Finally, a model for multicultural stakeholder participation in HIA is presented.

Research publications

(1) Negev, M. (2012). Knowledge, data and interests: Challenges in participation of diverse stakeholders in HIA. *Environmental Impact Assessment Review, 33*, 48-54.

(2) Negev, M., Levine, H., Davidovitch, N., Bhatia, R., & Mindell, J. (2012). Integration of health and environment through health impact assessment: Cases from three continents. *Environmental Research, 114*, 60-67.

(3) Negev, M., Davidovitch, N., Garb, Y., & Tal, A. (2013). Stakeholder participation in health impact assessment: A multicultural approach. *Environmental Impact Assessment Review, 43*, 112-120.

(4) Negev, M., & Teschner, N. (2013). Rethinking the relationship between technical and local knowledge: towards a multi-type approach. *Environmental Science and Policy, 30*, 50-59.

Early Fetal Loss: The Association between Air Pollution and other Major Risk Factors and Spontaneous Abortions in Southern Israel

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2009–2012

Pregnancy is a complex process that involves biological and environmental risk factors which may lead to undesirable outcomes. The scientific literature offers various reports on the incidence of spontaneous abortion (SA)/early fetal loss (EFL). Though there is evidence of the involvement of environmental risk factors in normal pregnancies, a connection is yet to be proven. The unique fertility patterns in the Negev area, the presence of the Ramat Hovav Industrial Park, and real-time air quality monitoring enable the study of a potential link between exposure to various air pollutants and environmental factors and SA/EFL among pregnant Negev residents. In order to assess the various risk factors that may affect SA or EFL among Negev residents, we carried out a case-control study at Soroka Medical Center among Jewish and Bedouin women whose verifiable pregnancy had terminated due to SA or EFL prior to the 22nd week of pregnancy. Those women were matched with a control group, which advanced past the 22nd week of gestation, based on ethnic origin and age. Personal exposure to various risk factors was evaluated by subject's place of residence, personal interviews and medical records.

Understanding Policy Change Sequences in Vehicle and Industrial Air Pollution Policies in Israel

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Supervisor
Eran Feitelson

2009–2012

The study deals with patterns of policy change in Israeli vehicle and industrial air pollution policies with the aim of mapping sequences of policy changes and understanding the factors and conditions affecting them. The study includes mapping policy changes in the first decade of the millennium, constructing a policy change timeline and analyzing policy change sequences. Mapping policy changes takes into account change magnitude and accumulation over time. Analysis of sequences takes into account the factors and conditions characterizing the policy areas which are consequential for change patterns such as resistance to change by stakeholders. Change patterns will also be compared to those in road safety policy which is generally characterized by relatively weak stakeholder resistance to change. Results from a three year timeline of policy changes (2002-2004) revealed the following: a significant phenomenon of accumulating changes in policy sequences; several central characteristics of policy sequences important for analysis; and a significant difference between the vehicle air pollution sequence and the industrial air pollution sequence.

Estimating Cancer Risk Attributed to Living in Proximity to Large Petroleum Storage Tanks

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Supervisors
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2009–2012

The relationship between exposure to petroleum products and their negative health effects is well established in occupational studies. However, the question remains whether living near petroleum storage facilities represents a cancer risk. In this study, age standardized rates (ASRs) and recently developed Double Kernel Density (DKD) tools were used to estimate relative risks of lung and non-Hodgkin's lymphoma (NHL) cancers attributed to residential proximity to the Kiryat Haim petroleum terminal. An innovative approach of exposure estimation using soil samples was also tested in Ashkelon. In contrast to the ASRs approach, the DKD approach was found to be a more sensitive tool, revealing that the relative density of both lung and NHL cancers declined in line with distances from the industrial zone, especially among the elderly. We conclude that living near petroleum storage sites may represent a significant cancer risk which cannot always be detected by traditional epidemiological approaches based on aggregated zonal estimates.

Research publications

(1) Zusman, M., Dubnov, J., Barchana, M., & Portnov, B.A. (2012). Residential proximity to petroleum storage tanks and associated cancer risks: Double kernel density approach vs. zonal estimates. *Science of the Total Environment, 441*, 265-276.

(2) Zusman, M., Ben Asher, J., Kloog, I., & Portnov, B.A. (2013). Estimating multi-annual $PM_{2.5}$ air pollution levels using sVOC soil tests: Ashkelon South, Israel as a case study. *Atmospheric Environment, 81*, 633-641.

(3) Portnov, B.A., & Zusman, M. (2014). Spatial data analysis using kernel density tools. In J. Wang (Ed.), Encyclopedia of business analytics and optimization (pp. 2252-2264). *Hershey, PA: Business Science Reference*. doi:10.4018/978-1-4666-5202-6.ch203

Integration of Satellite Observations and Ground Monitoring and its Application for Assessing Exposure to PM in Israel

Fellow

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Supervisor

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2011–2014

Particulate matter air pollution (PM) is usually characterized by its size and chemical composition, which may affect its diverse health effects. Recent studies, based on standard ground monitoring data, revealed significant associations between fine particles (diameter<2.5μm) and human health. Satellite-based observations can provide an answer to some ground monitoring limitations, since satellite imagery allows environmental mapping at a large spatial scale. This study examines how satellite observations can be used for gaining better understanding of regional air quality in Israel for deriving reliable human health risk metrics. Initially we are developing a dust classification model defining dust/anthropogenic PM sources. Furthermore, this work consists of retrieval of data from different sources, including a new high resolution product from NASA, and the development of methods for linking, integrating, and assimilating these databases. The work has merit not only from a scientific standpoint, as the results are expected to present additional tools for policy makers for introducing appropriate guidelines and regulations.

Research publications

(1) Sorek-Hamer, M., Cohen, A., Levy, R.C., Ziv, B., & Broday, D.M. (2013). Classification of dust days by satellite remotely sensed aerosol products. *International Journal of Remote Sensing, 34*(8), 2672-2688.

(2) Sorek-Hamer, M., Strawa, A.W., Chatfield, R.B., Esswein, R., Cohen, A., & Broday, D.M. (2013). Improved retrieval of $PM_{2.5}$ from satellite data products using non-linear methods. *Environmental Pollution, 182*, 417–423.

Index

Investigators

Topics

Adar, Sara D., 31
Afek, Arnon, 20
Agay-Shay, Keren, **51, 57**
Amitai, Yona, 23, **33**
Avnon, Lone, 27
Ayal, Adi, 26

Baccarelli, Andrea, 39
Barchana, Micha, 59
Bar-Ilan, Igal, 37
Ben-Ari, Julius, 32
Benenson, Itzhak, 28
Benor, Shira, **36**
Berkovitch, Matitiahu, **29**
Berkowitz, Brian, 17
Berman, Tamar, 15, 23, 29, 30, 32, 33
Bilenko, Natalya, **48**
Blumberg, Dan, 27, 57
Boyd Barr, Dana, 32
Brauer, Michael, 14
Britzi, Malka, 29
Broday, David, **14**, 22, 34, **35**, 36, 39, 60
Brook, Jeffrey, 41
Broza, Meir, 19
Brunekreef, Bert, 48

Calderon-Margalit, Ronit, 15, **30**
Chefetz, Benny, **15, 17, 32**
Chudnovsky, Alexandra, **43**
Cytryn, Eddie, **24**

Davidovitch, Nadav, 26, 58
Dayan, Uri, 18, 31
Doitsch, Elyakim, 21, 37
Dror, Ishai, 17
Drory, Aliza , **57**
Drory, Yaacov, 22, 36
Dubnov, Jonathan, 59
Dubowski, Yael, 14, **21**

Erel, Yigal, **18**
Ergaz-Shaltiel, Zivanit, 30
Ertl, Peter, 32
Eskenazi, Brenda, 15, 49
Etzion, Yael, 14

Factor-Litvak, Pam, 29
Farhi, Adel, 28
Feitelson, Eran, 59
Finkelstein, Yoram, **21**, 37
Fireman, Elizabeth, 36
Fishbain, Barak, 14, 39
Freeman, Shirra, **42**
Friger, Michael, 27, 57, 58
Frimer, Ron, 20

Garb, Yaakov, 58
Gerber, Yariv, **22, 34, 36**
Göen, Thomas, 33
Golan, Rachel, **52**
Goldsmith, Rebecca, 23
Greenberg, Nili, 20
Grotto, Itamar, **23**
Guerra, Stefano, 45
Gun, Jenny, **35**

Hadar, Yitzhak, 15, 17
Haimov-Kochman, Ronit, 30
Hammitt, James K., 42
Hareuveny, Ronen, 26
Hauser, Russ, 39, 46
Hoffmann, Barbara, 53

Kark, Jeremy D., **25**
Kashi, Yechezkel, **19**
Katra, Itzhak, **27**
Keinan-Boker, Lital, 25
Kivity, Shmuel, 36
Kloog, Itai, 38, **44**
Kordova, Levana, 18
Koren, Ilan, 34
Koton, Silvia, 22
Koutrakis, Petros, 14, 27, 43
Krispel-Ochayon, Riki, **58**

Lavi, Iris, **45**
Lerner-Geva, Liat, **28**
Lev, Ovadia, **35**
Leventer-Roberts, Maya, 33
Levin, Noam, 25
Levine, Hagai, 15, 25, **55**

Index **Investigators**

Levy, Amalia, 29
Levy, Ilan, 14, 25**, 39, 41**
Liberty, Idit F., 38
Linn, Shai, 57
Lubetzky, Ronit, 29

Machtinger, Ronit, **39, 46**
Mandel, Dror, 29
Manor, Orly, 15
Maor, Yehoshua, 15, 32
Marcus, Michele, 54
Mir, Debby, **37**
Moshe, Shlomo, 20
Myers, Vicki, 36

Negev, Maya, **37, 58**
Nieuwenhuijsen, Mark, 14, 51
Nirel, Ronit, **31**
Novack, Victor, 27, **38**

Paltiel, Ora, 15
Peled, Amatzia, 57
Peretz, Alon, 20, 31
Peretz, Chava, 57
Perez, Oren, **26**
Petrick, Lauren, **56**
Portnov, Boris A., 59

Raanan (Arnon), Rachel, **49**
Racowsky, Catherine, 39, 46
Rappaport, Stephen, 56
Raz, Raanan, **50**
Reznick, Abraham, 14
Richter, Elihu, 21
Roth, Zvi, 15
Rothen-Rutishauser, Barbara, 32
Rudich, Assaf, **38**
Rudich, Yinon, **20**, 28, **34**, 38

Sarnat, Jeremy, 14, 20, 52
Schauer, James, 14, 18, 38
Schwartz, Joel, 25, 44
Segal, Ehud, **59**
Segal-Rosenhaimer, Michal, 21
Shechter, Michael, 33
Shlezinger, Meital, 33
Shoham-Vardi, Ilana, 58
Shohat, Tamy, 23
Soback, Stefan, 29
Sorek-Hamer, Meytar, **60**
Sprecher, Hannah, 19
Stayner, Leslie, 15
Steinberg, David M., 22, 34
Stern, Eli, 28
Sunyer, Jordi, 51
Swan, Shanna, 15, 55
Sznitman, Josué, **32**

Tal, Alon, 58
Terry, Mary Beth, 47
Tobvin, Joseph, 29
Tordjman, Karen, **33**
Tzivian, Lillian, **53**

Vin-Raviv, Neomi, **47**
Vrijheid, Martine, 51

Wainstock, Tamar, **54**
Wanger, Arye, 18
Weisskopf, Marc, 50

Xing, Baoshan, 15

Yishai, Ruti, 19
Yitshak Sade, Maayan, 38

Zudman, Yuval, 14
Zusman, Marina, **59**

Agriculture, 14, 15, 17, 21, 24, 32

Air pollution, 14, 18, 20, 22, 25, 27, 28, 31, 32, 34, 35, 36, 37, 38, 39, 41, 43, 44, 48, 50, 52, 53, 57, 58, 59, 60
- air monitoring stations, 14, 20, 22, 28, 35, 38, 41, 43, 48, 50, 60
- carbon monoxide (CO), 39
- metals, 18, 48
- multipollutant mixture, 41, 52
- nitrogen oxides (NO_x), 20, 22, 25, 28, 38, 39 41, 48, 53, 57
- ozone (O_3), 28, 39, 41, 48
- particulate matter (PM) (*see* particulate matter)
- satellite-based estimates (*see* satellite-based estimates)
- sulfur dioxide (SO_2), 28, 38
- traffic-related air pollution, 20, 22, 25, 34, 35 38, 39, 48, 52, 57, 59
- volatile organic compounds (VOCs), 59
- wireless sensors (*see* wireless sensors)

Antibiotic resistance, 24

Asthma, 20, 36, 45, 49, 52

Autism spectrum disorder (ASD), 50

Bioassay, 18, 32

Biomarkers, 45, 49, 51, 52, 56

Biomonitoring, 23, 29, 30, 33, 51

Birth cohort study, 29, 48, 49, 51

Birth outcomes, 15, 28, 29, 30, 33, 44, 51, 57, 58
- anogenital distance, 29, 30
- congenital heart defects, 57
- congenital malformations, 28, 57
- early fetal loss, 58
- low birth weight, 28, 44, 51
- preterm birth, 28
- small for gestational age, 28
- spontaneous abortion, 58

Blood pressure, 48

Cancer, 25, 54
- breast cancer, 47
- colorectal cancer, 33
- leukemia, 56
- lung cancer, 59
- non-Hodgkin's lymphoma (NHL), 59

Cardiac health outcomes
- cardiovascular diseases (CVD), 31, 33, 42
- ischemic heart diseases, 27, 57
- myocardial infarction (MI), 22, 33, 34, 36

Case-control study, 50, 56, 58

Case-crossover study, 31

Cellular phones, 26

Children
- childcare products, 35
- children's environmental health, 15, 21, 28, 29 30, 33, 36, 37, 48, 49, 50, 51, 56, 57

Cognitive function, 21, 53

Cohort study, 22, 25, 28, 30, 34, 36, 47, 51, 53, 54, 57

Crossover study, 52

Cross-sectional study, 20, 21, 53

Desalinated drinking water, 33

Diabetes mellitus, 33, 38

DNA methylation, 47

Dust storms, 27

Endocrine disrupting chemicals (EDCs), 15, 23, 29, 30, 33, 35, 39, 46, 47, 51, 54
- bisphenol A (BPA), 23, 33, 39, 46, 51
- phthalates, 23, 29, 30, 33, 35, 39, 51

Environmental health policy, 26, 37, 58, 59

Epigenetics, 47

Exposome, 56

Fertility, 15, 46, 54, 55

Flame retardants
- brominated flame retardants (BFRs), 14, 29, 54
- polybrominated biphenyls (PBBs), 54
- polybrominated diphenyl ether (PBDEs), 51
- polychlorinated biphenyls (PCBs), 47

Food, 15, 23, 32, 33, 42

Frailty, 36

Geographic information system (GIS), 25, 28, 48, 50

Green spaces, 51

Health impact assessment (HIA), 58

Human oocyte (egg), 39, 46

In vitro fertilization (IVF), 46

Land use regression (LUR), 25, 48, 53

Longitudinal study, 34, 53

Metabolomics, 52, 56

Meteorological conditions, 14, 18, 31, 38, 41, 43, 50, 57

Methylmercury (MeHg), 42

Neurodevelopmental disorders, 21

Noise

- traffic noise, 48, 53

Non-ionizing radiation, 26, 56

Particulate matter (PM), 14, 18, 22, 25, 27, 28, 31, 32, 34, 36, 38, 39, 43, 44, 48, 50, 52, 53, 57, 60

- diesel engine particles (W-DEP), 38
- PM_{10}, 18, 27, 28, 38, 48, 50, 53, 57
- $PM_{2.5}$, 18, 22, 25, 27, 34, 36, 38, 43, 44, 48, 50, 52, 53
- toxicity, 18
- ultrafine particles (UFPs), 32, 36, 52

Pathogenic bacteria, 19

Pesticides, 14, 15, 21, 23, 30, 32, 37, 47, 49

- drift, 14, 21
- organochlorines, 47, 51
- organophosphates, 15, 21, 23, 30, 32, 37, 49

Pharmaceutical compounds, 15, 17

- carbamazepine, 15, 17
- crop uptake, 15, 17

Polycyclic aromatic hydrocarbons (PAHs), 23

Population based study, 22, 27, 53

Prenatal exposure, 28, 29, 30, 33, 47, 49, 50, 51, 56, 57

Reclaimed wastewater, 15, 17, 24

- antibiotic resistance (*see* antibiotic resistance)

Respiratory health outcomes

- asthma (*see* asthma)
- chronic obstructive pulmonary disease (COPD), 27, 45
- lung function, 45, 49
- respiratory diseases, 36, 49, 57

Risk assessment, 42

Satellite-based estimates, 34, 38, 43, 44, 60

Spirometry, 36, 49

Tobacco smoke, 14, 23, 45, 56

Weight

- low birth weight (*see* birth outcomes)
- obesity, 38
- overweight, 51

Wireless sensors, 14, 35, 39