

Pharmacotherapy in Changing Environmental Physical Activity (EPA). Preventive Measures

Eliyahu Stoupel

Division of Cardiology, Rabin Medical Center, Petah Tiqwa, Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

***Corresponding author:** Eliyahu Stoupel, Division of Cardiology, Rabin Medical Center, Petah Tiqwa, Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel, Tel: 972-97426439; Fax: 972-577-971684; Email: Stoupel@inter.net.il; EGStoupel@gmail.com

Citation: Eliyahu Stoupel (2017) Pharmacotherapy in Changing Environmental Physical Activity (EPA). Preventive Measures. Emerg Med Inves 2017; J131. DOI: 10.29011/2475-5605.000031

Received Date: 20 January, 2017; **Accepted Date:** 1 April, 2017; **Published Date:** 10 April, 2017

Abstract

In recent year's many studies were published related to a number of cardiovascular pathologies and, also, to Space Weather effects on human health-a part of Clinical Cosmobiology. These studies are related to close associated Solar (SA) and Geomagnetic Activity (GMA) and their Antagonist Cosmic Ray (CRA) (Neutron) Activity. At days of extreme high (Stormy-IV0) GMA such risk factors like arterial blood pressure, blood coagulation parameters, markers of inflammation (CRP), some immune system signs are rising. SA is inverse correlated to CRA $r=-0.85$, $p=0.0001$; GMA/CRA = $-0.66, 0.0001$; and SA/GMA are related by $r=0.55$, $p<0.0001$. Such important pathologies like Acute Myocardial Infarction (AMI) and some its serious complications, Sudden Cardiac Death (SCD), life threatening cardiac Arrhythmias (VF, VT, VES, AF) are related to low GMA (or Zero GMA) and High CRA (Neutron Activity).

Aim: The aim of this study is to discuss, if the prescribed to patients pharmacotherapy must consider the mentioned links and adjust the drug doses to the EPA and adapt them to changing, especially extreme Space Weather events.

Methods: The basis for this study were many decades of clinical comparisons of medical events and their outcomes with daily, monthly, yearly Space Weather activity, concomitant laboratory test results; comparison of data related to different levels of Space Weather Activity and discussion of adopted pharmacotherapy, if its possible.

Conclusion

- Presented data show that at days of extreme Space Weather activity many risk factors of Cardiovascular Disease are changing their levels.
- The question is, if fluctuating, in accord to Space Weather prediction, drug dose can be effective
- At days of high CRA (Neutron) activity the use of artificial magnetic fields by high risk patients is a possibility worth to check.
- At the days higher CRA (Neutron) activity more active measures against air pollution are recommended.

Keywords: Arrhythmia; Acute; Cosmic Ray; Coagulation; Cardiac; Events; Geomagnetic; Inflammation; Neutron Activity; Pharmacotherapy.

Introduction or Background:

Human life is accompanied by a number of Space Weather energetic fields. The Sun and related Geomagnetic field activities

serve as shields against possible harmful effects of Cosmic Ray activity that in extreme cases overlap all known limits of our Planet accepted highest limits of energy (1019 Electron-Volt.). Only the accepted now presumption that CRA has its source close to our, but separate galactic black hole and prevent us from revision of many parts of physics [1-11]. Many studies published in the XX and XXI centuries deal with biologic effects of SA, GMA [12-

43]. Since 1989 a term of Clinical Cosmobiology was introduced presenting events of Clinical Medicine in the time of changing EPA- Space Weather [22,23]. Studies related to General Health tendencies, Cardiovascular, Congenital, Psichiatric, Neurologic, Pregnancy and Genetic related events, Newborn morbidity, Ophthalmology related pathologies, Traumatology (including traffic accidents) Emergency Medicine, different forms of Sudden Cardiac Death, Endocrinology and many other were published [12-58]. If in the first years the dominant place in these studies were SA and GMA effects, in the last decades their antagonist CRA (and their close “partners” high energy (more 90MEV) Proton flux are more and more studied. [2-6,36-41]. It’s presumed that CRA related colossal energies affect atoms at the borders of our galactic, pressing their electrons back into the nucleus and transforming them to Neutrons. This give a marker of CRA - Neutron activity on our Planet’s surface in impulse per minute (imp/min). As it was mentioned in the abstract studies of the last decades show the correlation levels of SA and GMA $r=0.55$; and inverse relationship to CRA (Neutron) activity: SA/CRA= -0.85; GMA/CRA=-0.66 [39-41,23]. In the last years medical events at days of Zero GMA (accompanied by higher CRA (Neutron) activity) were studied and at following days were studied, trying to see situation when the predominant Space Weather force close to us are the Neutrons [39,46] Table 1.

Differences in some risk factor markers and clinical course at days of extreme Space Weather (GMA,CRA) Activity. The following table presents significant cardiovascular risk factors and morbidity-mortality rise at highest (Stormy, IV0) days of GMA and at lowest (Quiet, I0) days of GMA accompanied by high Neutron activity,

GMA Stormy Days	Low GMA -High CRA-Neutron Activity
Blood Coagulation	Electrical Heart Instability
1. Prothrombin time $p=0.007$ (INR) $\uparrow 11.18\%$	I0/IV0 GMA APB's $\uparrow 31.57\%$; VPB's $\uparrow 25\%$
2. Platelets Count $p=0.002$ $\uparrow 24.33\%$	VT, VF I0/ IV0 GMA: $r=0.97$; $p=0.02$
3. Fibrinogen $p=0.002$ $\uparrow 11.18\%$	\uparrow (more) PAF, AMI, SCD.
4. Platelets Activity $p=0.001$ $\uparrow 8.633\%$	Cardiac Arrhythmia in 14.1% AMI pts . I0/IV0 GMA $r=0.96$; $p=0.01$
5. Basophyl's $p=0.003$ $\downarrow 63.33\%$	Implantable Cardioverter Defibrillator (ICD) Discharges for VT, VF at 9246 ± 299 imp./min. Daily average at $1995-2005$ 8865 ± 411 imp/min; I9/IV0 GMA $r=0.96$. $p=0.01$
Inflammation	Stroke (CVA) mortality- Neutron Activity $r=0.41$, $p<0.0001$; (n-132020)

1. \uparrow C-reactive Protein IV0/ I0 $r=0.96$; $p=0.039$;	
2. \uparrow Immunoglobulins M,G;	
3. \uparrow Anti cardio lipin Syndrome	
Arterial Blood Pressure:	
1. Systolic press. $\uparrow 4.06$; Diastolic press. $\uparrow 2,246$ mm Hg;	
2. Maximal Daytime \uparrow Systolic press. 5.56 mm Hg.	
3. \uparrow Diastolic press. 6.04 mm Hg.	

Table 1: some cardiovascular disease risk factors in extreme (high/low) daily space weather conditions. [23]

Discussion

So, we have two groups of medical events related to high GMA, related to higher blood coagulation, inflammation, higher arterial blood pressure and the second group related to Low (Quiet) GMA and higher CRA (Neutron) activity and connected with electrical heart instability, cardiac arrhythmia's, sudden cardiac deaths, complications of intravascular atheroma (atherosclerotic plaque rupture, or fissuring (AMI), cerebral thrombosis and embolism or bleeding (CVA) [61-63]. How can Neutrons affect our body? It's presumed that Neutrons, included our tissues (inhaling, or other ways) are joining the H⁺ Anions, transforming to Protons and attacking our inside located heart conduction system, intravascular Atheroma's (rich by H⁺ Anions) [64,65]. Antagonists to the coagulation rising consequence are Anticoagulants (Warfarin-Coumadin, Heparin etc.), Antiplatelet drugs (Aspirin, Clopidogrel-Plavix, Prasugrel, Tipigralor etc.), New Anticoagulants (NOAC) like Dabigatran etc. Many groups of antihypertensive drugs are used for prevention of high blood pressure related artery damage and bleedings (CVA), myocardial strain, hypertrophy and Heart Failure (Beta-blockers, Angiotensin Converting Enzymes Antagonists and their Receptor Blockers, Diuretics, Calcium Antagonists etc.). It's of special importance in Diabetic patients, Dislypidermia suffering persons and other high risk groups. The question is, if some drug dose changes can be done having prediction of a strong GMA storm in the coming days. For example in anticoagulants, or antiplatelet drugs, antihypertensive treatment with blood pressure control that is today in available in many patients home.

As it was shown in a number of studies [27-31,33,35,37,39,40] higher GMA prevents a number of life threatening cardiac arrhythmias and connected SCD, One of the most popular cardiac events in all parts of the World. A relative short time ago it was shown that

under the influence of MRI (Magnetic Resonance Imaging) study (using magnetic field for diagnostics) the most untreatable Depression patients show improvement [59,60] in a number of studies; many MRI devices were transformed from diagnostic to therapeutic facilities. Cardiac arrhythmia in a big Mayo clinic arranged study (2016; ref.38) and in many of our studies [36,39,46,56-58] it was confirmed that higher GMA prevents severe, life threatening cardiac arrhythmias. In our previous studies it was mentioned that artificial magnetic fields can be used in an attempt to prevent life threatening cardiac arrhythmias. It's the time to make such attempts. The dosage of antiarrhythmic drugs can also be revised.

The possibility that extreme changes of Space Weather activity are provoking some changes in Gene activity, regulating many sites of human homeostasis were also discussed [66].

The problem is that still people studying Space Climate are usually working isolated from clinicians, often are physicists, or physicians, isolated from clinical practice. On the other hand most physicians are not familiar with the Space Weather elements, and don't have data about the changing daily energetic spectrum. We send a note, that, maybe, such changes are worth to check. An additional question was raised referring to such risk factors of cardiovascular disease like CRA (Neutron) activity and air pollution: we don't know precisely how the CRA related Neutrons surrounding our planet, as a marker of this Space Weather component, are joining our body cells and tissues. One of the ways that can be supposed is the connection of the Neutrons to the fine particles (nanoparticles) of air pollution and together invading our respiratory and other systems. The possibility at days of higher Neutron (CRA) level to put more efforts for prevention of contacts with polluted air (respirators, air filtration and other possibilities, in addition to global efforts to drop air pollution) [67-70]. Discussing such possibilities we must also remember that high GMA (Stormy) and Quiet days (accompanied by higher Neutron activity) are in the last decades distributed unequal: Quiet days (with higher Neutron activity) in years 1983-2007 were 41.62%, Stormy – 4.38%, in 1995-2010, Quiet days 57.75%, Stormy -1.68% [21].

Conclusion

1. Presented data show that at days of extreme Space Weather activity many risk factors of Cardiovascular Disease are changing their levels.
2. The question is, if fluctuating, in accord to Space Weather prediction, drug dose can be effective
3. At days of high CRA (Neutron) activity the use of artificial magnetic fields by high risk patients is a possibility worth to check.
4. At the days higher CRA (Neutron) activity more active measures against air pollution are recommended.

References

1. Heckman G (Ed) Glossary of Solar-Terrestrial Terms, NOAA, Space Environment Services Center, Boulder, Co, NOAA, USAF.
2. Sigl G (2001) Ultra-High –Energy Cosmic Rays: Physics and Astrophysics Science 291: 73-79.
3. Aharonian F, Akhperjanian AG, Bazer-Bachi AR, Belicke M, Benbow W, et al. (2006) Discovery of very-high - energy gamma rays from the Galactic Centre ridge. Nature 439: 695-698.
4. The Pierre Auger Collaboration (2007) Correlation of the highest-energy cosmic rays with nearby extragalactic objects. Science ss318: 938-943.
5. Dorman LI (2013) Cosmic Ray's as a factor and tool for forecasting of space weather influence on the biosphere. In "Space Weather effects on humans in space and on Earth" Space Research Institute. Moscow I: 92-109
6. Stoupel E, Israelevich P, Petrauskienė J, Kalediene R, Abramson E, et al. (2002) Cosmic Ray Activity and Monthly Number of Deaths: a Correlative Study. J Basic ClinPhysiolPharmacol 13: 23-32.
7. Preliminary Report and Forecast of Solar Geophysical Data. Weekly. Boulder. USA. Weekly NOAA-SESC (now SWPC), USAF.
8. Solar Indices Bulletin NOAA. National Geophysical Data Center, USA.
9. Geomagnetic Indices Bulletin NOAA, National Geophysical Center, USA. IZMIRAN, Russian Academy of Sciences.
10. Neutron Monitoring Data, Moscow Neutron Monitoring Station, Russian Academy of Sciences.
11. Neutron Monitoring Data (daily, monthly, yearly) Oulu University Finland
12. Tchijevsky Effects of the physical factors of nature on the nervous elements and the activity of the animals. Home report presented at the Zoo psychological laboratory, V., Moscow. Treatment of climatologie biologique et Medicale 1: 672 Paris.
13. Tchijevsky AL (1976) Terrestrial Echo of the Solar Storms. II - nd Ed. Misl. Moscow.
14. Sardon G and Faure M (1927) Tachessolaria and human pathology. The Medical Press 18. Paris
15. Budai E (1931) Tachessolaria and meningitis cerebrospinalis. Review of Pathology and General Hygiene 419. Paris.
16. Faure M (1934-1935) Cosmobiologie. Nice.
17. Barnothy JM (1964) in Biological effects of Magnetic Fields. Plenum Press, New York 1: 93.
18. Rozhdestvenskaya E, Novikova K (1969) The influence of solar activity on the blood fibrinolytic system. Med. Referative Journal 10: 65-69.
19. Oranevski VN, Breus TK, Baevski R, Rapoport SI, Petrov VM et al. (1998) Effect of Geomagnetic Activity on the Functional Status of the Body Biofizika 43: 819-826
20. Stoupel E, ES Babayev, E Abramson, J Sulkes (1976) Days of "Zero" level geomagnetic activity accompanied by the high neutron activity and dynamics of some medical events—Antipodes to geomagnetic storms. Forecasting in Cardiology. John Wiley & Sons, New York 1: 141.
21. Stoupel E (1980) Solar-Terrestrial Prediction: Aspects for Preventive Medicine. In Solar-Terrestrial Predictions Proceedings RF. Donnelly (Edit.) US NOAA, Space Environment Laboratory, Boulder, Co., 4: 29-41.

22. Stoupel E (1989) Clinical Cosmobiology. Newsletter of the Bio-Electro-Magnetic Institute. Spring. Boulder. Co. USA 1: 7-8.

23. Stoupel E Space Weather and timing of cardiovascular events. (Clinical Cosmobiology) 2012 Lambert Academic Publishing. Saarbrucken. 72p.

24. Stoupel E, Joshua H, Lahav J (1996) Human blood coagulation parameters and geomagnetic activity. *Eur J IntMed* 7: 217-220.

25. Stoupel E, Abramson E, Gabbay U, Pick AI (1995) Relationship between immunoglobulin levels and extremes of solar activity. *Int J Biometeorol* 38: 89-91.

26. Stoupel E, Monselize Y, Lahav J (2006) Changes in Autoimmune Markers of the Anti Cardiolipin Syndrome on Days of Extreme Geomagnetic Activity. *J Basic & ClinPhysiol&Pharmacol* 17: 269-278.

27. Stoupel E, Abramson EP, Sulkes J, Harell D (2007) Dynamics of serum C-reactive protein(CRP) and cosmophysical activity *Eur J Int Med* 2: 124-128

28. Stoupel E, Zabludovsky M, Wittenberg C, Boner G (1998) Ambulatory blood pressure monitoring in patients with hypertension on days of high and low geomagnetic activity. *Int J Hypertension* 39: 293-294.

29. Stoupel E, Hod M, Shimshoni M, Friedman S, Ovadia J (1990) Pregnancy induced hypertension in months with different cosmic activity. *ClinExperObstGynec* 17: 7-12.

30. Stoupel E, Keret R, Assa S, Kaufman H, Shimshoni M et al. (1983) Secretion of growth hormone, prolactin and corticosteroids during different levels of geomagnetic activity. *Neuroendocrinology Letters* 6: 365-358.

31. Stoupel E, Keret R, Gil-Ad I, Assa S, Silbergeld A, et al. (1980) Secretion of growth hormone and prolactin in extreme periods of solar activity in solar cycle 21 (1976-1986). *Neuroendocrinology Letters* 11: 191-295.

32. Khabarova OI, Dimitrova S (2008) Some proves of integrated influence of geomagnetic activity and weather changes on human health. *Space Physics*: pp306-pp309.

33. Vencloviene J, Babarskiene R, Milvidaite I, Kubilius R, Stasinyte J (2013) The effect of solar -geomagnetic activity during hospital admission on coronary events within 1 year in patients with acute coronary syndromes. *Advances in space research* 52: 2192-2198.

34. Gurfinkel YI (2004) Ischemic heart disease and solar activity. IIKC. "Elfi-3", Moscow 34.

35. Saposhnikov D, Revich B, Gurfinkel Y, Naumova E (2013) The influence of meteorologic and geomagnetic factors on acute myocardial infarction and brain stroke in Moscow, Russia. *Int J Biometeorol* 58: 1-12.

36. Stoupel E (1993) Sudden cardiac death and ventricular extrasystoles on days with four levels of geomagnetic activity. *J. Basic Clin. Physiol. Pharmacol* 4: 57-67.

37. Stoupel E, Domarkiene S, Radishauskas R, Bernotiene G, Abramson E, et al. (2004) Links between monthly rates of four types of acute myocardial infarction and their corresponding cosmophysical activity parameters. *J Basic & Clinic Physiol&Pharmacol* 14: 3-4.

38. Stoupel E, Babayev E, Mustafa F, Abramson E, Israelevich P, et al. (2007) Acute Myocardial Infarction Occurrence: Environmental Links - Baku 2003-2005 data. *Med Sci Monitor* 13: BR175-BR179.

39. Stoupel E, Tamoshunas A, Radishauskas R, Bernotiene G, Abramson E, et al. (2011) Neutrons and the Plaque: AMI (n-8920) at Days of Zero GMA/ High Neutron Activity (n-36) and the Following Days and Week. Kaunas, Lithuania, 2000-2007. *Clinical & Experimental Cardiology* 12: 121-125.

40. Stoupel E, Abramson E, Israelevich P (2011) Left anterior descending/right coronary arteries as culprit arteries in acute myocardial infarction (n-2011) in changing physical environment, percutaneous coronary intervention data (2000-2010). *J Basic ClinPhysiol Pharm*. 22: 91-96.

41. Stoupel E, Abramson E, Domarkiene S, Shimshoni M, et al. (1997) Space Proton Flux and the Temporal Distribution of Cardiovascular Deaths. *Intern J Biometeorol* 40: 113-116.

42. Stoupel E, Goldenfeld M, M, Shimshoni M, Siegel R (1993) Intraocular pressure (IOP) in relation to four levels of daily geomagnetic activity and extreme yearly solar activity. *Intern J Biometeorol* 37: 42-45.

43. Stoupel E, Kremer I, Mutmacher L, Abramson E, Yassur Y Acute Glaucoma and Retinal Detachment at four daily levels of geomagnetic activity . 11-th International Conf. High Power Electromagnetics EUOEM 98 Abstracts. P190. Tel Aviv.

44. Ebrille E, Konecny T, Spacek R, Konecny D, Jones P, et al. (2015) Correlation of Geomagnetic Activity with Implantable Cardioverter Defibrillator Shocks and Antitachycardia Pacing. *Mayo Clinic Proceedings* 90: 202-208.

45. Stoupel E, Domarkiene S, Radishauskas R, Bernotiene G, Abramson E, et al. (2004) Links between monthly rates of four types of acute myocardial infarction and their corresponding cosmophysical activity parameters. *J Basic & Clinic Physiol&Pharmacol* 14: 175-184.

46. Stoupel E, Babayev ES, Abramson E, Sulkes J (2013) Days of "Zero" level geomagnetic activity accompanied by the high neutron activity and dynamics of some medical events-Antipodes to geomagnetic storms *Health* 5: 1-7.

47. Stoupel E, Tamoshunas A, Radishauskas R, Bagdoniene G, Abramson E, et al. (2010) Acute myocardial infarction (AMI) and intermediate coronary syndrome (ICS). *Health* 2: 129-132.

48. a) Stoupel E, Radishauskas R, Vaichiulys V, Bernotiene G, Tamoshunas A, et al. (2016) Data about Natural History of Some Acute Coronary Events at Days of High Cosmic Ray (CRA) - Neutron Activity and Following 48 Hours. *Health* 8: 1-7.

49. Stoupel E, Abramson E, Domarkiene S, Shimshoni M, Sulkes J (1997) Space Proton Flux and the Temporal Distribution of Cardiovascular Deaths. *Intern J Biometeorol* 40: 113-121.

50. Stoupel E, Israelevich P, Gabbay U, Abramson E, Petrauskienė J, et al. (2000) Correlation of two levels of space proton flux with monthly distribution of deaths from cardiovascular disease and suicide. *J Basic ClinPhysiolPharmacol* 1: 63-71.

51. Stoupel E, Petrauskienė J, Gabbay U, Kalediene R, Abramson E, et al. (2001) Circannual Rhythmicity of Death Distribution. *Acta MedicaLithuanica* 8: 37-42.

52. Stoupel E (2014) Considering space weather forces interaction on human health. The equilibrium paradigm in Clinical Cosmobiology: is it equal?. *J Basic ClinPhysiolPharmacol* 26: 147-151.

53. Stoupel E, Kalediene R, SauliuneS, Abramson E, Shochat T, et al. (2015) Space weather and human deaths distribution: 25 years observation (Lithuania1989-2013). *J Basic ClinPhysiolPharmacol* 26: 1-9.

54. Stoupel E, Babayev E, Mustafa F, Abramson E, Israelevich P, et al. (2007) Acute Myocardial Infarction Occurrence: Environmental Links - Baku 2003-2005 data. *Med Sci Monitor* 13: BR175-BR179.

55. Stoupel E, Babayev ES, Mustafa FR, Abramson E, Israelevich P, et al. (2006) Clinical Cosmobiology - Sudden Cardiac Death and Daily / Monthly Geomagnetic, Cosmic Ray and Solar Activity - the Baku Study, (2003-2005). *Sun & Geosphere* 1: 13-16.

- 56. Stoupel E, Abramson E, Israelevich P (2011) Left anterior descending/ right coronary arteries as culprit arteries in acute myocardial infarction (n=2011) in changing physical environment, percutaneous coronary intervention data (2000-2010). *J Basic ClinPhysiol Pharm* 22: 91-95.
- 57. Stoupel E, Kusniec J, Mazur A, Abramson E, Israelevich P, et al. (2008) Timing of life-threatening arrhythmias detected by implantable cardioverter -defibrillators in relation to changes in cosmophysical factors. *Cardiology Journal* 15: 1-4.
- 58. Stoupel E, Kusniec J, Golovchiner G, Abramson E, Kadmon U, et al. (2014) Association of electrical heart storm occurrence with environmental physical activity. *Pace* 37: 1067-1070.
- 59. Stoupel E, Israelevich P, Petruskiene J, Kalediene R, Abramson E, et al. (2002) Cosmic Ray Activity and Monthly Number of Deaths: a Correlative Study. *J Basic ClinPhysiolPharmacol* 13: 23-42.
- 60. Grisaru N, Yaroslavsky U, Abarbanel J, Lamberg T, Belmaker RH (1994) Transcranial magnetic stimulation in depression and Schizophrenia Neuropsychopharmacol 3:287-288.
- 61. Kirsten Weir (2015) Can magnets cure depression?. American Psychologic Association 46: 50.
- 62. Maseri A, Fuster V (2003) Is there a vulnerable atherosclerotic plaque. *Circulation* 107: 2068-2073.
- 63. Libby P (2003) Vascular biology of atherosclerosis. *Circulation* 91: 56-64.
- 64. Stoupel E (2008) Atherothrombosis: Environmental Links. *J Basic ClinPhysiolPharmacol* 1: 135-145.
- 65. Nias AHW (1998) An introduction to radiotherapy. John Wiley & Sons: 64
- 66. Hall EJ, Giaccia AJ (2006) Radiotherapy for Radiologists, Lippincott and Wilkins & Williams, Philadelphia, Baltimore, New York, London, Buenos Aires, Hong Kong, Tokyo.
- 67. Stoupel E (2014) Gene functional dynamics: environment as a trigger. *J Basic ClinPhysiolPharmacol* 25: 129-132.
- 68. Brook RD, Franklin B, Cascio W, Hong Y, Howard G, et al. (2004) AHA Scientific Statement :Air pollution and cardiovascular disease. *Circulation* 109: 2655-2671.
- 69. Stoupel E (2016) Cosmic ray (neutron) activity and air pollution nanoparticles- cardiovascular disease risk factors-separate or together?. *J Basic ClinPhysiolPharmacol* 27: 1-4.
- 70. WHO (2014) Ambient (outdoor) air quality and health. Fact Sheet.
- 71. Miller KA, Discovick DS, Shepperd K, Sullivan JH, Anderson GL, et al. (2007) Long-term exposure to air pollution and cardiovascular events in woman. *N Engl J Med* 356: 447-458.