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Relações entre meio ambiente urbano e qualidade de vida:

Um estudo a partir do caso da poluição do ar

Tese apresentada à Faculdade de Medicina da Universidade de São Paulo, para obtenção do título de Doutor em Ciências

Programa de Fisiopatologia Experimental

Orientador: Prof. Dr. Paulo Hilário Nascimento Saldiva

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Aos meus país sempre,

e também à minha querida cidade

natal que aprendi a amar profundamente.

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“As melhores respostas guardam perguntas”

(Frase proferida durante aula da pós-graduação,

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NORMATIZAÇÃO ADOTADA

Esta tese está de acordo com as seguintes normas, em vigor no momento desta publicação:

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Universidade de São Paulo. Faculdade de Medicina. Divisão de Biblioteca e Documentação. *Guia de apresentação de dissertações, teses e monografias*. Elaborado por Anneliese Carneiro da Cunha, Maria Julia de A. L. Freddi, Maria F. Crestana, Marinalva de Souza Aragão, Suely Campos Cardoso, Valéria Vilhena. 3ª Ed. São Paulo: Divisão de Biblioteca e Documentação; 2011.

Abreviaturas dos títulos dos periódicos de acordo com *List of Journals Indexed in Index Medicus*.

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LISTA DE ABREVIATURAS E SIGLAS

CAPES	Coordenadoria de Aperfeiçoamento de Pessoal de Nível Superior
FAPESP	Fundação de Amparo a Pesquisa do Estado de São Paulo
FMUSP	Faculdade de Medicina da Universidade de São Paulo
IARC	Agência Internacional de Pesquisa sobre Câncer
IEA	Instituto de Estudos Avançados
IPCC	Painel Intergovernamental sobre Mudanças Climáticas
MP_{10}	Material particulado com diâmetro aerodinâmico menor que 10 micrômetros
$M_{2.5}$	Material particulado com diâmetro aerodinâmico menor que 2.5 micrômetros
OMS	Organização Mundial da Saúde
USP	Universidade de São Paulo

RESUMO

Fajersztajn L. *Relações entre meio ambiente urbano e qualidade de vida: um estudo a partir do caso da poluição do ar*. [tese]. São Paulo: Faculdade de Medicina, Universidade de São Paulo; 2016.

As cidades são hoje o habitat natural da espécie humana. Grande parte dos fatores de risco que mais contribuem para o adoecimento são altamente prevalentes nas cidades e são modificados pelo meio ambiente e estilo de vida urbanos, como poluição do ar, falta de saneamento básico, baixos níveis de atividade física, entre outros. Modificações no uso e ocupação do solo, ciclos geoquímicos, clima, sistemas hídricos e biodiversidade, em curso nas cidades, já as caracterizam como um ecossistema particular. Ecossistemas urbanos são complexos. Cada intervenção urbana acarreta uma série de efeitos na cidade, nem sempre previsíveis ou desejáveis, de modo que a governança urbana é um dos principais desafios de desenvolvimento do século XXI. Neste estudo procuramos entender algumas relações entre cidade e qualidade de vida, partindo do caso da poluição do ar. Postulamos que seria possível produzir artigos científicos de bom nível que permitissem integrar diferentes áreas de conhecimento numa linguagem adequada a um publico mais amplo, a fim de orientar formadores de opinião, gestores públicos e órgãos legislativos desejosos de estimular políticas voltadas para a promoção da qualidade de vida. Nesta tese apresentamos na íntegra oito artigos científicos produzidos sobre cidades e qualidade de vida que conduzimos ao longo deste estudo, divididos em quatro tipologias: 1) Estudos a partir da análise de dados secundários; 2) Estudo na ausência de dados secundários sistematizados, 3) Estudo a partir de revisão sistemática e metanálise e 4) Narrativas para públicos diversos. Sete estudos já foram, de alguma forma, publicados. Para fins desta tese, concluímos que é possível produzir artigos científicos de bom nível que integrem conhecimentos científicos de diferentes áreas do conhecimento numa linguagem compreensível para gestores e demais interessados em políticas voltadas para a promoção da qualidade de vida urbana.

Descritores: cidades; cidades saudáveis; metrópoles; saúde da população urbana; qualidade de vida; poluição do ar; monitoramento ambiental; neoplasias pulmonares; saúde pública.

ABSTRACT

Fajersztajn L. *Links between urban environment and quality of life: the case of air pollution.* [Thesis]. São Paulo: "Faculdade de Medicina, Universidade de São Paulo"; 2016.

Cities are today the natural habitat of human beings. Most of the leading risk factors for the global burden of disease are highly prevalent in cities and are partially shaped by urban life style and the built environment (e.g. ambient air pollution, unsafe sanitation, low physical activity levels, among others). Changes in land use and cover, geochemical cycles, climate, hydrosystems and biodiversity are current in course in cities, thus cities can be considered a particular ecosystem. Urban ecosystems are complex, each urban intervention results in a wide range of effects, not all predicable or desired at fist. Urban governance is a major development challenge of the XXI century. In this study, we looked for selected links between cities and quality of life, focusing at first on air pollution-related issues. In this thesis we investigated if it was feasible to produce high quality scientific papers that integrate different scientific topics through a narrative suitable for a broader public: decision-makers and other actors interested in evidence-based urban polices for better quality of life. In this thesis, we depict the full text of eight scientific papers on urban health related issues produced during this post-graduation, seven of which already published. Papers are presented according to the following typologies: 1) Studies that used secondary data analysis, 2) Dealing with scarcity of secondary data, 3) Systematic Reviews and Meta-analysis and 4) Narratives for a wider public. We concluded that producing high quality scientific papers that integrate different scientific topics throughout a comprehensive language for a broader public interested in evidence-based urban polices for better quality of life in urban settlements is feasible.

Descriptors: cities; health city; metropolis; urban health; quality of life; air pollution; environmental monitoring; lung neoplasms; public health.

1. INTRODUÇÃO

O domínio das técnicas de produção de alimentos foi determinante para que a maior parte dos seres humanos deixasse a vida nômade. A passagem do extrativismo para a agricultura mais sistematizada e a mudança da caça para a domesticação de animais, foram os elementos centrais para a nucleação de grupos de seres humanos, primeiramente em vilas com dúzias ou talvez centenas de pessoas que se conheciam e, posteriormente, em cidades com milhares de pessoas. A partir do progressivo exercício criativo do espírito humano, que produziu ofícios, corporações, guildas, comércio, arte e conhecimento, as cidades, por sua vez, foram os núcleos formativos das metrópoles, caracterizando a criação de um ecossistema muito particular. Com milhares/milhões de habitantes, as metrópoles impõem um desafio de convívio que, durante a maior parte da existência humana como espécie, era resolvido através da separação e formação de grupamentos humanos distintos[(1)]. No ecossistema das metrópoles, o adensamento populacional e a ausência de saneamento se acentuaram, criando condições propícias para o adoecimento, o qual, de certa forma, nublou o encantamento da urbanidade. A malária, a febre amarela, o tifo, e, atualmente, as novas doenças infecciosas, tem parte de suas biografias impressas no alfabeto esculpido pelos tijolos urbanos. Mais recentemente, temas como a violência do tráfego ou da criminalidade organizada e a formação de periferias desprovidas de infraestrutura onde as condições sanitárias retrocedem o viver para séculos anteriores, nublam ainda mais o encantamento da urbanidade. Ademais, a exclusão social, a imobilidade das artérias congestionadas das metrópoles, as ilhas de calor, a poluição "à moda dos fuzileiros navais (pelo ar, pelas águas, pelo solo)" e o rejuvenescimento de doenças infecciosas (também conhecidas por reemergentes), acrescentaram um pouco mais de *Pathos* (no sentido da caixa de

Pandora) às cidades e subtraem delas um pouco mais do *Logos*. Em resumo, a saúde escapa da caixa da saúde, como se um Prometeu moderno fosse punido em um penhasco de concreto de um arranha-céu urbano, de forma a indicar que a gestão deste novo ecossistema depende de interações complexas.

As cidades são hoje o habitat natural da espécie humana e vieram para ficar. Mais da metade da população mundial vive em cidades e as projeções são de aumento contínuo[2,3]. O ecossistema urbano já é a realidade do habitat de 80% da população latino-americana[3] e 84% da população brasileira[4]. O crescimento das cidades altera a paisagem, os ciclos geoquímicos, o clima, os sistemas hídricos e a biodiversidade[5–7]. Alimentar e fornecer energia e bens de consumo para tantos habitantes urbanos já é a principal causa das mudanças climáticas globais[2,8,9]. Vejamos alguns exemplos específicos das conexões do meio ambiente urbano e qualidade de vida dos seus habitantes. Morar próximo a um parque pode reduzir o risco de infarto do miocárdio, ao passo que a exposição à poluição do ar ambiente aumenta o risco[2,10–13]. Trocar a cobertura verde da cidade por asfalto e construir arranha-céus, interfere no microclima urbano, o que por sua vez, aumenta eventos extremos de temperatura e altera o regime de chuvas[14,15]. Se outrora São Paulo foi a terra da garoa, hoje enfrenta períodos alternados de enchente e seca. Os extensos congestionamentos de veículos aumentam a concentração de poluentes atmosféricos, o que também interfere no microclima da cidade[14], além de prejudicar diretamente a saúde humana com efeitos negativos que vão desde ardor nos olhos e crises de asma até câncer de pulmão e morte[13,16–25]. A imobilidade do tráfego em São Paulo subtrai o tempo que os habitantes urbanos dispõem para outras atividades como sono, lazer, educação e autocuidado, a um custo anual estimado em mais de 40 bilhões de reais[24]. A opção pelo carro como meio de transporte, em detrimento ao transporte ativo (caminhar ou andar de bicicleta como

parte ou na completude da jornada ao destino final), de um lado contribui para a poluição do ar local e para uma maior emissão de gases de efeito estufa, e de outro contribuem para o aumento do sobrepeso e obesidade na população[25,26]. Soma-se a isso, o crescente número de evidências científicas associando a exposição crônica ao ruído do tráfego a alterações cardíacas, distúrbios do sono, entre outros prejuízos à saúde[27–29]. Em 2014, mais de mil pessoas morreram no trânsito de São Paulo[30]. No entanto, recomendar que as pessoas fiquem em casa com as janelas fechadas é inviável[10]. A adoção de hábitos saudáveis pode ser favorecida ou dificultada pelo ambiente construído e pelo modo como a cidade está organizada[31–33]. Além disso, alguns fatores de risco para doenças, independem ou dependem muito pouco de escolhas individuais, mas sim de ações governamentais[10,11].

No ecossistema urbano quem determina se um local vai abrigar um parque ou um prédio, ou se um rio vai dar lugar a uma avenida, não são as regras clássicas da natureza, são regras ditadas pelo sistema de gestão das cidades[34], que sofrem influência de valores culturais e econômicos que mudam muito rapidamente. Sendo assim, as Nações Unidas[3] tem destacado a governança urbana como o desafio de desenvolvimento central no século XXI.

Recentemente, a Science dedicou uma edição inteira mostrando que cidades são sistemas complexos, que o mundo já está urbanizado e que a governança das cidades afetará de forma determinante as gerações futuras[2]. No campo específico da Saúde, a comunidade científica tem mostrado que políticas de baixo carbono, advogadas internacionalmente como fundamentais para enfrentar as mudanças climáticas, também reduzem a poluição do ar local e trazem benefícios para a saúde populacional[35–44]. Tais políticas, tem sido advogadas como a principal oportunidade para promover a saúde global no século XXI[39,40]. Desde 1987 a Rede Europeia de Cidades Saudáveis,

hospedada na Organização Mundial de Saúde (OMS), de certa forma reconhece esta oportunidade e reúne cidades comprometidas com a saúde e com o desenvolvimento sustentável. A cada cinco anos, a rede seleciona temas específicos para discussão e ação. Na primeira fase a iniciativa contava com 35 cidades com o objetivo comum de introduzir novas formas de pensar e promover cidades saudáveis. Hoje com cerca de 100 cidades, a rede está na fase VI, cujas metas são: 1) melhorar a saúde de todos os cidadãos e reduzir as inequidades de saúde e 2) aprimorar a liderança e a participação na governança de saúde[45].

Iniciativas semelhantes são raras na América Latina e no Brasil. Tomemos como exemplo a poluição do ar. A despeito do aumento exponencial das evidências sobre os impactos negativos dos poluentes atmosféricos na saúde humana[13,17,18,21–23], a poluição do ar persiste em muitas regiões do mundo e aumenta em algumas regiões do Brasil e América do Sul[46]. Nos últimos anos o Brasil presenciou avanços importantes na melhoria da qualidade do ar, como a eliminação do uso do fogo durante o processo de colheita de cana de açúcar em áreas mecanizáveis no Estado de São Paulo[*]. No entanto, também testemunhou retrocessos, como a suspensão, em 2014, da inspeção veicular ambiental iniciada em 2009 no município de São Paulo e o projeto de lei em tramitação que libera a fabricação e comercialização de carros a diesel[†].

Formada em Fisioterapia, fui treinada a olhar de frente problemas (deficiências, incapacidades e dores dos pacientes) muitas vezes negligenciados pela sociedade. Fui também treinada a identificar as potencialidades remanescentes dos pacientes, como

[*] O Protocolo Agroambiental do Setor Sucroenergético, é um acordo voluntário assinado em 2007 pelo Governador de São Paulo, pelos Secretários de Estado do Meio Ambiente e de Agricultura e Abastecimento e pelo presidente da União da Indústria Sucroalcooleira que antecipou o fim da desespalha da cana por meio do uso de fogo para 2014 (nas áreas mecanizáveis, para todas as unidades industriais signatárias) e 2017 (áreas não mecanizáveis), além da recuperação de matas em nascentes e a proteção das áreas de preservação de outros cursos d'água.

[†] Projeto de Lei no 1.013/2011.

suas condições musculares, e trabalha-las para obtenção de um melhor desempenho funcional. Com o tempo fui percebendo que o modo de vida urbano e a cidade construída influenciavam a qualidade dos resultados de tratamento para níveis muito além daqueles que aprendi na graduação. Um exemplo clássico é a frequência semanal do tratamento, sempre desafiada pela difícil mobilidade na cidade de São Paulo, ou ainda, o agravamento dos sintomas respiratórios durante os dias mais poluídos. Esses desafios me levaram a procurar respostas sobre as relações entre saúde e cidade no terceiro setor, onde, à semelhança do meu treinamento em Fisioterapia, comecei a olhar para para alguns problemas da cidade, de certa forma também neglicenciados, e a tentar identificar potencialidades que pudessem auxiliar na resolução dos mesmos. No terceiro setor desenvolvi trabalhos em conjunto com o Laboratório de Poluição Atmosférica Ambiental da Faculdade de Medicina da Universidade de São Paulo. Reconhecido internacionalmente pelos seus estudos toxicológicos, clínicos e epidemiológicos em escala local e regional, o laboratório tem contribuição determinante para a liderança global da Universidade de São Paulo entre as 15 que mais publicam sobre poluição do ar e saúde no mundo[*]. Frente a tanto conhecimento produzido, percebi que, embora o papel da ciência nas sociedades democráticas da atualidade seja guiar os debates e informar a tomada de decisão sobre assuntos relevantes de interesse público[(47)], a transformação do conhecimento científico em melhores decisões políticas não ocorre de forma natural[(48)]. Em concordância com Lorente e Álvarez-Herranz[(49)] e outros autores[(50–52)], me convenci que a poluição ambiental não vai desaparecer sozinha, conforme o crescimento econômico e, que a qualidade ambiental, depende de políticas públicas. O mesmo vale para outras exposições urbanas que influenciam a saúde humana.

[*] Pesquisa realizada em 03 de maio de 2016 na plataforma on-line Scopus. Termos de busca: “air pollution” e “health”, filtro “Affiliation”.

Dado a complexidade da relação entre urbanidade e qualidade de vida, entrei na pós-graduação a fim de adquirir habilidades que me permitissem integrar os diferentes saberes inerentes ao entendimento dos sistemas urbanos, seguindo os objetivos expostos a seguir.

2. OBJETIVOS

A hipótese do presente estudo foi que seria possível produzir artigos científicos de bom nível* que, ao mesmo tempo, permitissem integrar diferentes áreas de conhecimento e orientar formadores de opinião, gestores públicos e órgãos legislativos desejosos de estimular políticas voltadas para a promoção da saúde e qualidade de vida. Como o tema em si é por demais amplo, utilizei como plataforma central o tema da poluição atmosférica, problema notório de saúde pública e, cuja resolução demanda o entendimento de várias áreas do conhecimento e, portanto, um típico exemplo de integração de saberes e políticas de cunho multi e transdisciplinar.

Os objetivos específicos deste doutoramento foram sendo construídos no decorrer do estudo, na medida do progressivo desenvolvimento das minhas habilidades, como também as de meu orientador. Neste período, o objeto de estudo em si – a poluição do ar – também se alterou. Por exemplo, muitos dos desfechos adversos de saúde associados à poluição, como o câncer do pulmão, passaram do nível de incerteza para o de certeza e se deslocaram para o ambiente urbano. Os objetivos específicos do presente estudo serão definidos no corpo de cada uma das publicações, as quais são, de fato, o corpo desta tese, e estão descritas na seção de Resultados.

* Definidos para fins deste estudo como aqueles publicados em periódicos que utilizam análise por pares.

3. MÉTODOS

Para testar a hipótese deste estudo, eu e meu orientador, entendemos que era necessário não só produzir ciência, como também suas correspondentes narrativas. Para fins deste estudo, definimos narrativa como uma interpretação de achados científicos construída de forma que um público geral tenha a possibilidade de compreendê-las.

Testamos a hipótese deste estudo a partir de um conjunto de publicações, por vezes diferentes em suas metodologias científicas formais, mas conectadas pelo mesmo tema - urbanidade e qualidade de vida - e também pelo foco na construção de suas respectivas narrativas voltadas para um público mais abrangente, como definido no primeiro parágrafo desta seção. Deste modo, os estudos foram sendo desenvolvidos a partir dos desdobramentos de uma primeira pergunta: "países com maior produção científica sobre poluição do ar e saúde respiram ar de melhor qualidade?". Em concordância com os objetivos, os métodos foram sendo construídos no decorrer do estudo, na medida do progressivo desenvolvimento das minhas habilidades, como também de meu orientador. Por exemplo, quando passei minha pós-graduação do mestrado para o doutorado direto, acordei com meu orientador que eu aprenderia técnicas de revisão sistemática e metanálise, fundamentais para aprimorar a sumarização e interpretação de evidências científicas. Deste modo, descreveremos a seguir as principais interações e capacitações que viabilizaram as publicações resultantes deste estudo.

Como capacitação, eu realizei disciplinas não só na Faculdade de Medicina da Universidade de São Paulo (FMUSP), mas também em diferentes unidades da Universidade de São Paulo (USP) como, Faculdade de Saúde Pública, Faculdade de Filosofia Letras e Ciências Humanas e Faculdade de Direito. A fim de aprofundar meus

conhecimentos em epidemiologia, fui monitora de disciplinas introdutórias da área nos níveis de graduação e de pós-graduação e hoje integro a direção da rede de Estudantes e Novos Pesquisadores da Sociedade Internacional de Epidemiologia Ambiental[*]. Destaco que conclui uma especialização de um ano em Revisão Sistemática e Metanálise, oferecida pelo Departamento de Patologia da FMUSP e um curso de curto período de introdução ao geoprocessamento com o programa Terra View Política Social.

Como meios de interação em nível institucional, destaco a articulação com a estrutura do Instituto de Estudos Avançados (IEA) da Universidade de São Paulo e minha experiência prévia no terceiro setor. Em nível pessoal, interagi com toxicologistas, geógrafos, epidemiologistas, médicos, climatologistas, estatísticos e biólogos, especializados em poluição do ar, desigualdades sociais, entre outros. Destaco ainda interações internacionais com pesquisadores das universidades de Harvard e Queensland. Muitos desses contatos foram cruciais para a minha formação e resultaram em parcerias de estudo, como evidenciado pela coautoria dos manuscritos apresentados na seção de Resultados.

A descrição específica dos métodos utilizados em cada um dos estudos que compõe esta tese está no corpo dos mesmos (vide seção de Resultados). Quando ausentes, pode-se considerar revisão critica de literatura como metodologia.

Por fim destaco que este estudo foi aprovado pelo Comitê de Ética em Pesquisa da Faculdade de Medicina da Universidade de São Paulo, em sessão de 06/06/2012, Protocolo de Pesquisa nº 162/12 (vide seção de Anexos, Anexo A).

[*] Dirigida por 13 jovens pesquisadores do mundo inteiro, rede é conhecida pelo seu nome em inglês: The Students and New Researchers Network (SNRN). Para mais informações vide o site da Sociedade Interncaional de Epidemiologia Ambiental: http://www.iseepi.org/About/snrn.htm

4. RESULTADOS

Durante a pós-graduação, eu produzi conhecimento científico e suas correspondentes narrativas a partir de pesquisa original, da avaliação e sumarização do conhecimento científico já produzido e também utilizando e analisando dados secundários para a construção das narrativas. Para fins desta tese, eu e meu orientador dividimos os estudos em quatro tipologias:

4.1. Estudos a partir da análise de dados secundários

4.2. Estudo na ausência de dados secundários sistematizados

4.3. Estudo a partir de revisão sistemática e metanálise

4.4. Narrativas para públicos diversos

A seguir, descrevemos as quatro tipologias e apresentamos os manuscritos correspondentes na forma em que foram publicados, ou na forma em que foram preparados para publicação. Uso a primeira pessoa para descrever os manuscritos. No entanto meu orientador foi fundamental para elaboração de todos os estudos e correspondentes narrativas. Também contei com a colaboração fundamental de outros pesquisadores durante a condução do estudo, como mostrado na autoria dos manuscritos, e fui coautora de um dos manuscritos.

4.1. Estudos a partir da análise de dados secundários

Nesta tipologia analisei dados secundários públicos para construir narrativas sobre dois assuntos relacionados à urbanização e saúde: a) poluição do ar e câncer e b) co-benefícios para a saúde advindos de politicas de baixo carbono no setor de transportes.

4.1.1. Poluição do ar e câncer

No artigo sobre poluição do ar e câncer[53] realizei uma revisão dos principais estudos longitudinais relacionando exposição à poluição do ar e câncer. O câncer foi escolhido como a doença de interesse porque no momento em que estava conduzindo o estudo, o IARC* discutia se a poluição do ar era carcinogênica para humanos, o que de fato se confirmou poucos meses depois[54,55]. A revisão demonstrou que os principais estudos foram realizados na Europa e América do Norte. A Ásia também contribuía com alguns estudos relevantes, mas os demais continentes, onde se concentram a maioria dos países em desenvolvimento, não tinham estudos com essas características. A revisão ainda mostrou que, no geral, o risco era significativamente aumentado, porém pequeno, comparado a outros agentes potencialmente modificáveis, como a fumaça do tabaco. A fim de construir uma narrativa mostrando que apesar de relativamente baixo, a poluição do ar era um fator de risco importante para o câncer, usei dados secundários para mostrar a exposição global à poluição do ar por densidade populacional e apresentei a informação visualmente, num mapa global. Para a construção da narrativa, também mostrei visualmente que os países com maior produção científica sobre poluição do ar e saúde, no geral, apresentavam melhor qualidade do ar. Comparei a produção de ciência sobre poluição do ar e saúde com a produção de ciência sobre

* IARC corresponde à sigla em inglês que designa a Agência Internacional de Pesquisa sobre Câncer, vinculada à Organização Mundial da Saúde.

outros fatores de risco ambientais importantes para saúde, cujas projeções para as próximas décadas são de declínio: malária e qualidade da água. O mapeamento dessa informação foi fundamental na construção da narrativa. O artigo foi publicado numa revista de alto impacto (JCR* 37,912 em 2013), mostrando que a uma narrativa bem construída usando revisão da literatura e dados secundários no momento certo é uma estratégia eficiente de publicação. Até julho de 2016 o artigo contava com 32 citações na plataforma *Web of Science* (mantida pela Thompson Reuters). A publicação na *Nature Reviews Cancer* demonstra que consegui construir uma narrativa sobre poluição e câncer para um público mais geral, notadamente oncologistas. O estudo recebeu o prêmio "2013 DOW *Sustainability Innovation Student Challenge Award"*, concedido pela Universidade de São Paulo, em parceria com a companhia química Dow. A publicação deste artigo foi o meu principal argumento para pleitear a mudança do projeto de mestrado para doutorado direto, o que foi concedido pelo Programa de Pós-Graduação em Fisiopatologia Experimental, considerando a recomendação da Banca Julgadora do Exame de Qualificação do Mestrado em 2013 e de meu orientador. A seguir apresento o artigo na íntegra.

* JCR é a sigla em inglês para Journal Citation Report, uma avaliação anual do impacto e desempenho das revistas internacionais realizada pela Thompson Reuters.

Artigo publicado

SCIENCE AND SOCIETY

Air pollution: a potentially modifiable risk factor for lung cancer

Laís Fajersztajn, Mariana Veras, Ligia Vizeu Barrozo and Paulo Saldiva

Abstract | Economic growth and increased urbanization pose a new risk for cancer development: the exposure of high numbers of people to ambient air pollution. Epidemiological evidence that links air pollution to mortality from lung cancer is robust. An ability to produce high-quality scientific research that addresses these risks and the ability of local health authorities to understand and respond to these risks are basic requirements to solve the conflict between economic development and the preservation of human health. However, this is currently far from being achieved. Thus, this Science and Society article addresses the possibilities of expanding scientific networking to increase awareness of the risk of lung cancer that is promoted by air pollution.

Determining the contribution of potentially modifiable risk factors (also known as cause-specific analysis for cancer) is crucial to implement cancer-preventive health policies[1]. Air pollution — household air pollution from burning solid fuels (for heating and cooking) and ambient particulate matter — was listed as one of the ten leading risk factors for the global burden of disease in 2010 (REF. 1). Most of these diseases are due to respiratory and cardiovascular events[2–5], but cancer is also an important outcome[1,3,5–11]. Lung cancer has the most robust association with prolonged exposure to air pollution, particularly when pollution is expressed in terms of particulate matter or gaseous components of air pollution. In fact, as exposure to higher concentrations of particulate matter increases, lung cancer becomes proportionally more important than cardiovascular events to the burden of disease[11]. For lung cancer mortality, excess risks rose nearly linearly throughout the full range of exposure to particulate matter, with a median aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$; fine particulate matter), whereas the slope of the curve for cardiovascular mortality was less steep. Currently, 8% of global lung cancer deaths can be attributed to exposure to fine particulate matter alone[3], although this estimate can be much higher (12.8%; confidence interval (CI) 95% = 5.9–18.5) if fine particles that are generated from human activity (as determined from satellite-derived assessments) are taken into account[12]. The dose–response relationship relating lung cancer and ambient particulate matter might be higher then previously estimated, particularly if only adenocarcinomas of the lung are considered. A recent European report that combined 17 long-term cohort studies in nine European countries identified a risk of 1.55 per 5 μg per m^3 of $PM_{2.5}$ (hazard ratio 1.55; 95% CI = 1.05–2.29)[51]. There is also a growing body of evidence that associates air pollution exposure to an increased risk of cancer in other tissues, such as the breast[13–16], haematopoietic tissues[17,18] and the urinary tract[7,19–22].

Air pollution and global burden of disease

Exposure to outdoor air pollution is expected to become the top environmental cause of premature mortality globally by 2050, overtaking malaria and water quality, which are traditional environmental risks for premature deaths, and the numbers of deaths from both of these are expected to fall over the same period[23]. The effect will be greater in developing countries that are not members of the Organization for Economic Cooperation and Development (OECD): these countries include Brazil, Russia, India, Indonesia, China and South Africa (BRIICS), as well as developing countries in the rest of the world[23]. There are densely populated regions in the world that have high air pollution concentrations (FIG. 1), especially megacities of developing nations. Fast urban and industrial development in these countries has resulted in growing demands for energy and rising expectations of material goods[24]. Therefore, megacities combine both concentrated emissions of air pollutants and large numbers of exposed people[25]. On a minor scale, hot spots of vulnerability can even occur in developed urban settings[26]. It is important to note that most of the epidemiological evidence relating air pollution to lung cancer has reported a linear dose–response effect[3,9,10,27–35,51] (TABLE 1). However, these studies were carried out in the United States[3,9,10,31,32] or Europe[27–30,51], which are areas with substantially lower levels of air pollution than those of developing countries. Studies in areas with higher pollution levels and high population levels are scarce[33–35] (TABLE 1) and are badly needed. Thus, this Science and Society article addresses the possibility of expanding scientific networking to increase awareness of the risk of lung cancer that is promoted by air pollution, especially in areas of the world where pollution is likely to be a substantial risk factor for lung cancer development and death.

Air pollution and cancer risk

Although the relative risk of developing cancer as a result of exposure to air pollution is generally small, the attributable risk (relative risk multiplied by the number of exposed people) is high, transforming ambient air pollution into the most significant environmental risk factor for lung cancer[1]. Indeed, lung cancer burden from air pollution is probably underestimated. Most of the long-term exposure studies for this pollutant have been carried out in areas where annual average concentrations range between 5 μg and 35 μg per m^3; however, the average concentrations of particulate matter in the major population centres of China, India and other developing countries are often much higher, and can exceed 100 μg per m^3 according to recent estimates[25].

Specific pollutants or complex mixtures?

Particulate matter can be considered as a mixture of air pollution sources that are present in the urban atmosphere rather than as a single pollutant. Particulate matter represents a complex mixture of solid and liquid components, which can vary substantially in composition and size depending on the emission source and prevailing weather conditions[36]. The composition and size of these particles determine the potential for deposition in the respiratory tract and the health effects that are associated with exposure[37]. Particles are classified according to their size, which can range from 0.005 μm to 100 μm in diameter. The smaller the size of the particle the greater its potential to penetrate deep into the respiratory tract[36].

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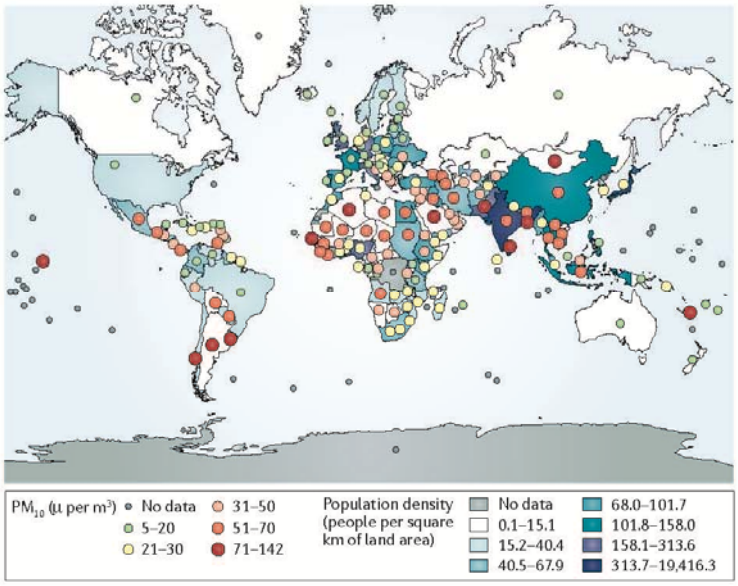

Figure 1 | **Global annual mean PM_{10} concentrations in 2009 by population density.** The map compares the population density in 2009 (data from the World Bank[49]) with the annual mean concentration of particulate matter of 100 µm or less (PM_{10}) in 2009 (data from the World Bank[50]).

The composition of these particles includes different classes of organic and inorganic chemicals, such as heavy and transition metals, organic compounds, hydrocarbons, ions, condensed reactive gas products and microorganisms. At higher concentrations the particles can also include microorganismal products (such as endotoxins), nitrates, sulphates and elemental carbon. Some of these particulates, such as polycyclic aromatic hydrocarbons, are known carcinogens[37,38]. Recently, diesel emissions, a substantial contributor to urban particles, were considered to be class I carcinogens by the International Agency of Research on Cancer[38], meaning that there is scientific evidence of carcinogenicity in humans.

In European and some Asian studies, significant associations were obtained relating lung cancer risk to gaseous components of air pollution, such as NO_2 and SO_2 (REFS 28–30,34,35). NO_2 has been shown to be a good indicator of traffic-related pollution[39], and SO_2 can be used to estimate diesel and industrial emissions. It is important to note that large cohort studies on lung cancer and air pollution rely on measures of specific pollutants. However, the atmosphere contains many compounds with known carcinogenic potential, such as polycyclic aromatic hydrocarbons and heavy metals, levels of which are not routinely measured. Thus, in such a complex mixture, it is difficult to ascribe the responsibility of causing lung cancer to a single component. Until a clear pathogenetic mechanism is defined, it would be prudent to consider the pollutants mentioned above as possible substitute markers of sources of air pollution, such as traffic or industrial pollution.

Air pollution control

The National Ambient Air Quality Standards (NAAQS), set up in the United States as part of the Clean Air Act, has been effective in controlling air quality[40], and it is a policy that has been recommended by the World Health Organization since 1987 (REF. 41). The stringency of air pollution control procedures varies substantially worldwide[42]. Indeed, a comprehensive global analysis that reviewed the 24-hour NAAQS for PM_{10} (particulate matter with a median aerodynamic diameter of less than 10 µm) revealed a positive correlation between the stringency of the NAAQS and the average annual exposure to PM_{10}, meaning that less stringent air quality standards lead to higher air pollution concentrations[42]. Efforts to control the sources of ambient air pollution should be considered a public health strategy to reduce lung cancer incidence, similar to the strategies that apply to tobacco and asbestos.

The process of reducing the use of asbestos and tobacco raised considerable public health controversies, which were driven by political, economic and individual liberty arguments. In the case of air pollution, the adoption of effective policies to control emission levels will be conceivably more challenging, as these policies will call into question our present use of energy and our apparently unbreakable dependence on personal motorized vehicles. Energy production — including oil and thermoelectric power — and the automobile industry represent enormous economic interests, and 'modern life' is based on increased energy use, which has become incorporated into our culture. Thus, a reduction in particulate matter levels will demand a considerable behavioural change. Traffic is one of the major sources of particulate matter[39]. Substantial technological advances have improved the efficiency of the nineteenth century internal combustion engine, leading to a reduction of air pollution concentrations. However, although air pollution from motorized vehicles has decreased in cities in Europe and North America as a result of more efficient petrol and diesel engines, it has not decreased as much as was hoped[25]. This is because the increase in road traffic and the resulting decrease in vehicle velocity are offsetting the gains that have been made by better car technology. In São Paulo, Brazil, particulate matter concentrations were decreasing progressively from 1996 to 2004, but they have remained unchanged since 2004 (REF. 43), indicating that technology alone will not be a solution if the numbers of vehicles and their intensity of use continue to increase. The same is true for the generation of electricity based on fossil fuels (coal, petroleum and gas); 40% of the electricity produced worldwide is currently generated from the combustion of coal, and this percentage is expected to rise in the next few decades as worldwide energy demands increase[44]. Thus, this will offset any improvements to levels of particular matter that have been gained through the use of modern thermoelectric power plants[45,46]. Moreover, the technological benefits of more advanced combustion engines and energy generation processes are not evenly distributed across the globe. One particularly difficult challenge is to tackle the lack of access to clean energy and the dependence of many people in low-income settings on inefficient and inadequately ventilated burning of biomass for household energy needs[44,47,48]. In this scenario, there are links between indoor and outdoor sources

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Table 1 | **Key studies relating air pollution to lung cancer**

Study	Setting	*N* (follow-up period)	Pollutant considered	Estimated risk	Adjustments
Europe					
Beelen *et al.*[27]	Netherlands	111,378 (1986–1997)	Black smoke concentration	RR (95% CI) = 1.47 (1.01–2.16) for never smokers; 0.91 (0.68–1.23) for ex-smokers; and 0.85 (0.70–1.03) for current smokers	Age, sex, smoking status and SES
			Black smoke (10 μg per m^3)	RR (95% CI) = 1.03 (0.78–1.34)	
			NO_2 (30 μg per m^3)	RR (95% CI) = 0.86 (0.57–1.29)	
			$PM_{2.5}$ (10 μg per m^3)	RR (95% CI) = 0.65 (0.41–1.04)	
			SO_2 (20 μg per m^3)	RR (95% CI) = 1.01 (0.67–1.54)	
Brunekreef *et al.*[28]	Netherlands	120,000 (1987–1996)	Black smoke (10 μg per m^3)	RR (95% CI) = 1.03 (0.88–1.20)	Age, sex, smoking status and SES
			NO_2 (30 μg per m^3)	RR (95% CI) = 0.91 (0.72–1.15)	
			$PM_{2.5}$ (10 μg per m^3)	RR (95% CI) = 1.06 (0.82–1.38)	
			SO_2 (20 μg per m^3)	RR (95% CI) = 1.00 (0.79–1.26)	
Cesaroni *et al.*[29]	Italy	1,265,058 (2001–2010)	NO_2 (10 μg per m^3)	HR (95% CI) = 1.04 (1.02–1.07)	Age, sex, marital status, place of birth, education, occupation and area-based socioeconomic position
Heinrich *et al.*[30]	Germany	4,800 (1980–2008)	NO_2 (16 μg per m^3)	HR (95% CI) = 1.25 (0.72–2.17)	Age, smoking status and education
			PM_{10} (7 μg per m^3)	HR (95% CI) = 1.97 (0.59–6.57)	
Raaschou-Nielsen *et al.*[51]	Nine European countries	312,944 (mean of 12.8 years)	PM_{10} (10 μg per m^3)	HR (95% CI) = 1.22 (1.03–1.45) for all lung cancers; 1.51 (1.10–2.08) for adenocarcinomas of the lung	Age, sex, smoking status and SES
			$PM_{2.5}$ (5 μg per m^3)	HR (95% CI) = 1.18 (0.96–1.46) for all lung cancers; 1.55 (1.05–2.29) for adenocarcinomas of the lung	
North America					
Dockery *et al.*[31]	United States	8,111 (1974–1991)	$PM_{2.5}$ (18.6 μg per m^3)	AMR (95% CI) = 1.37 (0.81–2.31)	Age, sex, smoking status, education, occupational exposure and medical history
Jerrett *et al.*[32]	United States	22,905 (1982–2000)	$PM_{2.5}$ (10 μg per m^3)	HR (95% CI) = 1.44 (0.98–2.11)	Forty-four individual level covariates, including income, race and SES
Krewski *et al.*[9]	United States	1,200,000 (1999–2000)	$PM_{2.5}$ (10 μg per m^3)	HR (95% CI) = 1.142 (1.057–1.234)	Forty-four individual level covariates, including income, race and social factors
Pope *et al.*[3]	United States	1,200,000 (1979–1983)	$PM_{2.5}$ (10 μg per m^3)	RR (95% CI) = 1.08 (1.01–1.16)	Age, sex, smoking status, marital status, education, occupational exposure, race, BMI, alcohol consumption and diet
		1,200,000 (1999–2000)	$PM_{2.5}$ (10 μg per m^3)	RR (95% CI) = 1.13 (1.04–1.22)	
		1,200,000 (1982–1998)	$PM_{2.5}$ (10 μg per m^3)	RR (95% CI) = 1.14 (1.04–1.23)	
Turner *et al.*[10]	United States	188,699 (1979–1983)	$PM_{2.5}$ (10 μg per m^3)	HR (95% CI) = 1.15 (0.99–1.35)	Age, sex, passive smoking, marital status, education, occupational exposure, race, BMI, diet, prevalent lung disease and radon exposure
		188,699 (1999–2000)	$PM_{2.5}$ (10 μg per m^3)	HR (95% CI) = 1.27 (1.03–1.56)	
		188,699 (1982–2008)	$PM_{2.5}$ (10 μg per m^3)	HR (95% CI) = 1.19 (0.97–1.47)	
Asia					
Cao *et al.*[33]	China	70,947 (1991–2000)	SO_2 (10 μg per m^3)	ΔM (95% CI) = 4.2 (2.3–6.2)	Age, sex, smoking status, education, BMI, alcohol consumption, physical activity and hypertension
Kantanoda *et al.*[34]	Japan	63,520 (1974–1983)	$PM_{2.5}$ (10 μg per m^3)	HR (95% CI) = 1.23 (1.09–1.38)	Age, sex, smoking status, diet and indoor charcoal or briquette braziers used for heating
			SO_2 (10 μg per m^3)	HR (95% CI) = 1.19 (0.97–1.45)	
			NO_2 (10 μg per m^3)	HR (95% CI) = 1.15 (1.06–1.24)	
Yorifuji *et al.*[35]	Japan	14,001 (1999–2009)	NO_2 (10 μg per m^3)	HR (95% CI) = 1.20 (1.03–1.40)	Age, sex, smoking status, BMI, hypertension, diabetes, financial capability and area mean income

AMR, adjusted mortality rate ratio; BMI, body mass index; CI, confidence interval; ΔM, percentage increase in mortality; HR, hazard ratio; $PM_{2.5}$, particulate matter with a median aerodynamic diameter of less than 2.5 μm; PM_{10}, particulate matter with a median aerodynamic diameter of less than 10 μm; RR, relative risk; SES, socioeconomic status.

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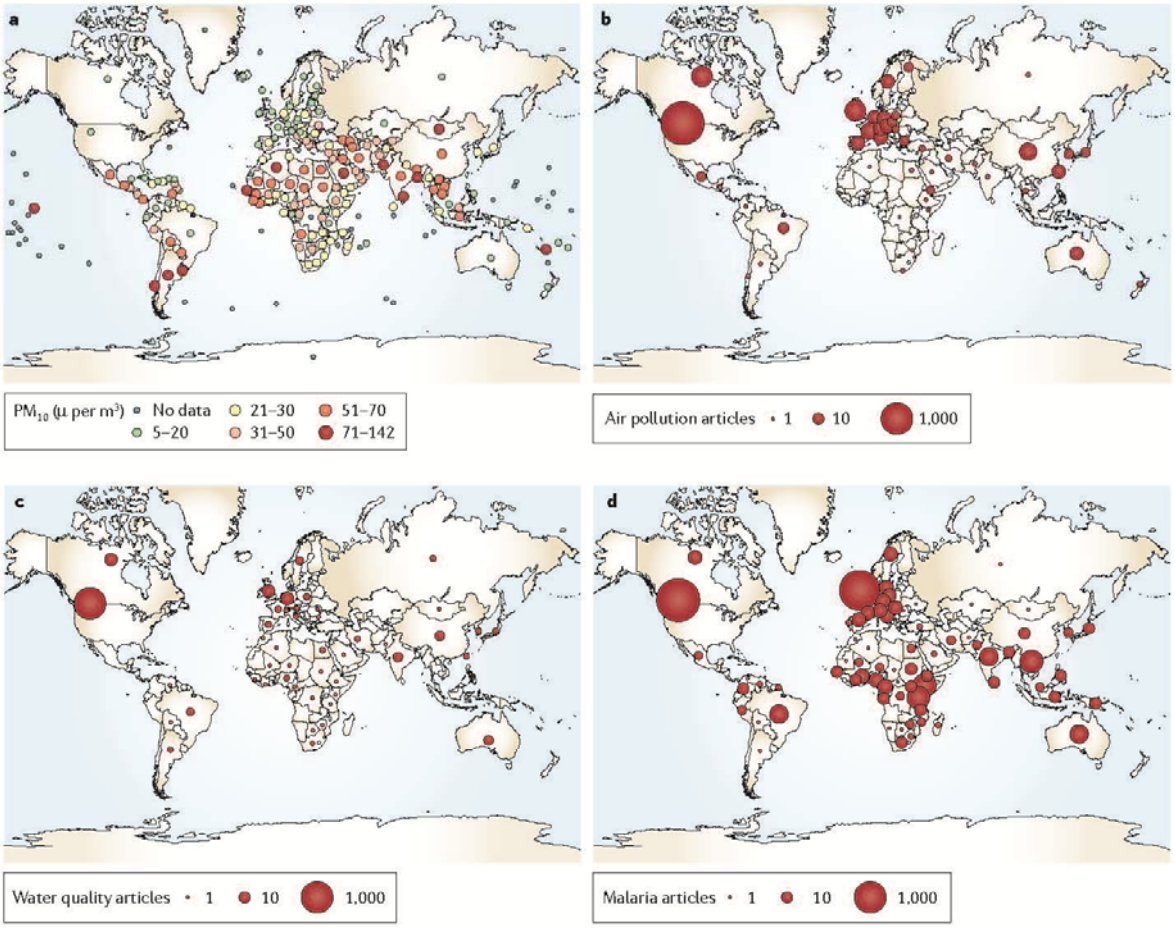

Figure 2 | **A comparison of scientific research output on various global health issues.** Global annual mean PM_{10} (particulate matter with a median aerodynamic diameter of less than 10 µm) concentration (µg per m³) in 2009 (part **a**)[49]. Number of articles in environmental public health published between March 1983 and March 2013 on air pollution (part **b**), water quality (part **c**) and malaria (part **d**), according to data from the Web of Science database. Search terms used were air pollution (part **b**), water quality (part **c**) and malaria (part **d**). The public environmental and occupational health filter was used for all searches.

of pollution, as a substantial proportion of outdoor air pollution may derive from poor household fuel combustion, particularly in Asia[44].

Science-based control of air pollution?

Theoretically, good scientific research is necessary to provide the basis for the implementation of policies that aim to control harmful environmental agents, helping society to decide a course of action once the apparent dilemma between preservation of human health and economic growth becomes more widely appreciated. In fact, governments that have a greater expenditure on health care have more stringent air quality standards, probably because of greater governmental awareness of the adverse health effects of air pollution and the consequent establishment of air pollution control measures to avoid increased health costs[42]. In this context, it would be interesting to know whether there is enough scientific research in air pollution hot spots to drive public policies that aim to reduce the problem. FIGURE 2 depicts a comparative panel of the number of papers produced from 1983 to date on malaria, water quality and air pollution, using the Web of Science database. There is a marked imbalance between levels of air pollution and local scientific production: a more balanced scenario emerges when waterborne diseases and malaria are considered. Developing rest of the world countries contribute to almost 20% of all the research on water quality and to approximately 70% of the research on malaria, but to only 5% of all air pollution papers. A 2012 report from the World Meteorological Organization[25] about the effects of megacities on air pollution and climate identified 11 international collaborative research projects, but only 50% focused on developing regions.

Conclusions and future directions

Sources of air pollution are unequivocally linked to economic activities; therefore, it is important to devise strategies to increase the collaboration between developed and developing nations to address the health effects of air pollution. Gains in scientific

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knowledge and global partnerships were effective in reducing the cancer risks associated with other environmental health issues, such as tobacco smoke and asbestos. Is now the time to do the same for air pollution?

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Competing interests statement
The authors declare no competing financial interests.

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4.1.2. Co-benefícios para a saúde advindos de politicas de baixo carbono no setor de transportes

Este manuscrito combina propriedades de um estudo e de uma narrativa e pretendeu apontar as desigualdades dos efeitos dos poluentes sobre a saúde sob a ótica da defasagem tecnológica entre países em desenvolvimento e países desenvolvidos. Usei dados secundários para mostrar visualmente a razão entre consumo de energia *per capita* (expresso pelas emissões *per capita* de CO_2) e concentração média de poluição local (expressa pela concentração média anual de MP_{10}[*]) por país. Esse conceito foi apresentado no Congresso da Sociedade Internacional em Epidemiologia Ambiental realizado em São Paulo em 2015 e publicado na forma de resumo[56]. Para o manuscrito, construí uma narrativa focada na América Latina e nos potenciais co-benefícios para a saúde populacional da região resultantes da adoção de políticas de baixo carbono no setor de transportes, particularmente melhor eficiência energética nos processos de combustão do setor de transportes. O manuscrito está em fase final de submissão e é apresentado a seguir, logo após apresentação do resumo apresentado na Conferência da Sociedade Internacional de Epidemiologia Ambiental.

[*] MP_{10} refere-se ao poluente atmosférico material particulado com diâmetro aerodinâmico menor que 10 micrômetros.

Resumo apresentado em Conferência.

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Program Oral Session – 02/09/2015 – 16h00-17h30 Air pollution and environmental justice

2757 - IMPROVING ENERGETIC EFFICIENCY IN DEVELOPING ECONOMIES: OPPORTUNITIES TO REDUCE GLOBAL HEALTH DISPARITIES

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Decarbonitization policies seem to have different size-effect on local health benefits, according to the development stage of the nation. High technological efficiency contributes to improvements in fossil fuel combustion process, reducing both greenhouse gas (GHG) and local pollutants emissions. The health gains are likely to benefit more people living in developing countries, where inefficient combustion technologies and bad air quality preponderate. Despite evaluations from the economic perspectives, no study has examined the role of technological inefficiency in global health inequality. In this study, we developed a global index to verify the magnitude of the technology inefficiency of energy production processes in the inequality burden of air pollution exposure. Methods. The index is the ratio of local air pollution level to GHG emissions by country: PM10/CO2. (Indicators: annual mean concentration of particulate matter of 10 μm or less in micrograms per cubic meter (PM10) and carbon dioxide (CO2) emission in metric tons per capita from manufacture of cement and burning of fossil fuel). We examined the

Sperman correlations between the index and the development status of the country (indicators: Gross National Income per capita, Atlas method (GNI), Human Development Index (HDI)), and the life expectancy. We also addressed the index trends from 1991 to 2010. Data were collected from the World Bank and The United Nations Development Program. Results. The index correlated significantly (p=0.001) with life expectancy (r=-0. 738), GNI (r=-0.883), and HDI (r=-0.868). The index trends indicate that developing economies decrease the ratio more rapidly than developed ones, but they are still far from the international standards for local pollutants. Conclusions. The index underlines that, improving technological efficiency in developing economies may be in an instrument to reduce global health inequalities from air pollution exposure.

Artigo em processo de submissão.

Combining low carbon transportation polices and human health: a global overview focused in Latin America.

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Abstract

The transport sector leads (37%) the dioxide carbon (CO_2) emissions from fossil fuel combustion in Latin America, and thus is an important focus of climate change mitigation. Low carbon polices in the transport sector yield large, immediate public health benefits due to their potential to reduce air and noise pollutants. Health net gains also emerge from the potential to reduce the risk of traffic-related injuries, to increase physical activity levels, among others. Despite the decrease in the growth of emissions rates, developed economies are still major CO_2 emitters, compared to all Latin American countries. At the same time, the quality of the air is usually better in the developed major CO_2 emitter countries, compared to most of Latin American countries. The mismatch might be a reflection of differences in technology of fossil combustion process. Improved technologies -highly prevalent in developed economies- release less particulates per CO_2 emissions, benefiting health. We proposed a global index that underline the contribution of technological inefficiency for the bad air quality in developing countries (Latin America inclusive), despite relatively lower GHG emissions. Given the high burden for health of ambient pollutant, the index might reflect health inequalities from technological inefficiency in fossil fuel combustion processes. Compare to the world, air quality and CO_2 emissions in Latin America figure in an intermediary scenario and there is room for improvements. Latin America is a highly urbanized continent, where many cities combine elevated levels of air pollutants,

large numbers of exposed people and relatively less stringent emissions standards for the transport sector, enhancing the health benefits of low carbon transportation polices. Transportation polices should be considered an environmental and a health police.

Key words: climate change, global climate change, air pollution, air quality, health, Latin America, CO_2 emissions, particulate matter, low carbon policy, environmental policy, health policy

Low carbon transportation can tackle climate change and improve health

Limiting climate change requires substantial and sustained reductions of greenhouse gas (GHG) emissions, particularly carbon dioxide (CO_2) emissions, 90% of the total anthropogenic GHG emissions in 20101. The transport sector leads (37%) the CO_2 emissions from fossil fuel combustion in Latin America[2], and thus is an important focus of climate change mitigation in the region.

Low carbon polices in the transport sector yield large, immediate public health benefits.

In part because these polices reduce GHG emissions and local ambient air pollutants levels (responsible for 4.3 million deaths in 20123) at the same time. Health net benefits also emerge from potentially traffic-related reductions in noise levels, risks for injuries, physical inactivity levels, among others[4].

Environmental, transportation and health policies are usually segregated by distinct sectors in urban administrations. However cities are complex and dynamic systems and all sectors influence each other. Decision-making for the best well-being of population and natural systems depends on overcoming segmentation. In this article we depict scientific evidence from several research areas to explain why transportation should also be considered an environmental and a public health police. Moreover, we propose a global index to highlight the higher burden of air pollution for developing and relatively low CO_2 emitter economies, compare to developed relative high CO_2 emitter ones.

GHG emissions and local particulate pollution in the world and in Latin America.

Cumulative emissions of CO_2 largely determine global mean surface warming and are already impacting natural and human systems all over the world[1].The energy sector contributed with 68% of the anthropogenic GHG emissions in 2010, most of each

resulting from the oxidation of carbon in fuels during combustion. In 2013, the transport sector leaded the CO_2 emission from fossil fuel combustion (37%) in Latin America[2].In other regions of the world, electricity and heat production were the major contributors sectors, but transportation also played a relevant role: 28% in developed countries, 23% in Middle East countries and 8% in China[2].

According to climate scientists, tackling climate change safely will require near zero emissions of CO_2 by the end of the century and substantial emissions reductions from all sectors –transport inclusively- over the next few decades[1]. However the world total CO_2 emissions increased 56% between 1990 and 2013[1].The rise of developed countries was far smaller, compared to developing nations (9% against 112%)[1]. Fewer population growth, more stringent emission standards and improvements in combustion technology explain in part the decrease in emissions rates. Latin American increase (104%) was slightly below developing countries mean, but smaller than Middle East and China rise (208% and 307% respectively)[2]. Low carbon policies for the transport sector are crucial to revert the risen trend and meet CO_2 reductions targets, particularly in Latin America. Hence, some polices encompasses net benefits for health and for the economy.

Particulate matter is a complex mixture of solid and liquid components, usually classified according to their size as coarse PM_{10} (ranging from 10 μm to 2.5 μm in diameter) and fine $PM_{2.5}$ (smaller than 2.5 μm in diameter)[5]. The composition and size of the particles are determined by the emission source and prevailing weather condition[5]. The smaller the size of the particle, the greater its potential to penetrate deep into the respiratory tract and the more severe its impacts for health[6]. The composition of particulates includes different classes of organic and inorganic chemicals, with different known toxicological effects for health[5], but have being widely used as an indicator of the real world exposure to air pollutants. Despite the variance in its composition, in 2013 the International Agency of Research on Cancer classified the particulate matter from outdoor air pollution carcinogenic for humans.

Long-term effects of air pollution for health also includes chronic pulmonary obstructive disease. Short-term exposure to particulates adversely affects mortality[3-4,6-7] and morbidity[4], notably from cardiovascular and respiratory causes in vulnerable populations (elderly, children, pregnant women, people with an existing chronic disease and low income populations). Endocrine, neurocognitive and other systems are also

negatively affected by particulates.

Developing countries depict higher levels of particulate pollution, compared to developed countries[9]. The highest concentrations are in Asia[9]. Latin America figures in an intermediary scenario[9]. This picture reflects differences in the burden of disease due to air pollution exposure among different regions of the world[3]. In 2012, 3.7 million premature deaths were attributable to ambient air pollution globally, 936 thousands occurred in South-East Asia, 176 thousands in Africa, 58 thousands in Latin America and 14 thousands in high income countries of the Eastern Mediterranean[3].

Technological inefficiency as a driver of higher burden of air pollution-related diseases.

Oxidation of carbon in fuels during combustion is a major contributor of the GHG emissions[2]. However, the particulate matter released -which impairs health-, depends on the quality of the combustion process. Driven by more stringent emission standards, developed countries are progressively shifting to lower-emissions vehicles that yield less particulate pollution. Older more polluting vehicles are being exported to developing country markets, where regulatory controls on fuels and vehicle maintenance are usually less strict[4]. As a result, particulate matter concentrations, and the health burden from them, are usually higher in low and middle income economies, compared to developed ones. Moreover, developing regions are undergoing a rapid urbanization and population growth, exposing more people to the health burden of air pollution.

Some studies, have evaluated the economic effects of technological improvements in motor vehicles, but its impact on health and equity are barely mentioned. High local particulate levels per CO_2 emission might reflect the technologic inefficiency of fossil fuel combustion processes in developing economies. We propose a global index to underline the contribution of technological inefficiency of fossil fuel combustion for the bad air quality, despite relatively low GHG emissions levels. Given the high burden for health of ambient pollutant[3-5,6-7], the index might reflect health inequalities from inefficiency of fossil fuel combustion process. The index is the ratio of local air pollution level (indicator: national mean concentration of coarse particulates[8]) to GHG emissions (indicator: CO_2 emissions per capita[9]) by country, or PM_{10}/CO_2. The human

developing index was used to address developing stages of the countries[10]. For the same amount of energy consumption (expressed by CO_2 emissions), low and middle income countries tended to emit more local particulate pollutants, compared to high income economies (Figure 1). In Latin America the index is higher compared to high income economies and lower compared to low and middle income ones (Figure 2). Given the high burden for health of ambient air pollution[3,6], improving technological efficiency of fossil fuel combustion in developing economies may be in an instrument to reduce global health inequalities. Low carbon transportation polices would greatly benefit environment and human health in the Latin America Latin, where the transportation is the major emitter sector.

Low carbon transportation polices and health

Health benefits related to the reduction in air pollution levels

Lower levels of air pollution have positive impacts in mortality and morbidity rates and largely explain the mechanisms of the health co-benefits of low carbon transportation polices. A study conducted in nine Latin American cites found small but significant short-term effects of PM_{10} levels on mortality[7], consistent with European and North American studies. Local evidence on fine particulate and long-term effects of air pollution is scarce in the region.

Stringent restrictions on motor vehicle use imposed during the Beijing Olympics, reduced fine and coarse particulate concentrations by 31% and 35% respectively[11].Asthma outpatient visits dropped nearly 50%[11]and the birth weight of full-term babies increased significantly[12]. Low carbon transportation polices related to local air pollution reductions include active transportation, smart land use, rapid public transportation and fuels choices (sources and emissions standards)[4,13].

Active transportation (travel by foot and/or bicycle on their one, or as part of a public transport journey) reduces air pollution because it reduces themiles travelled by private motorized vehicles[4,13]. In five Latin American cities (Cidad de México, Rio de Janeiro, São Paulo, Buenos Aires and Santiago), bike-shearing programs increased the number of cyclists[15]. Bike paths increased bicycle trips in Rio de Janeiro, Lima and Bogotá[4,15]. Land-use policies that reduce the distance of trips and restrict motor vehicle

concentrations depicted similar effects[4,13].An aesthetically pleasing walking environment can favour the adoption of active transportation, strength social support networks, and potentially mitigate heat waves from climate change, if combine with a densely green coverage[4,13].

Air pollution concentrations differ by public transport mode. Levels are higher in diesel bus, followed by subways and tram. Within subways, closing the window of the trains reduce air pollution exposure. Time of the journey is as important as concentration to determine human exposure to air pollutants. In Latin America, Bus Rapid Transit systems (BRT) were implemented in six cities[4,14] and also might be contributing to increase physical activity levels among those living close to BRT stations[4,14].

Although diesel vehicles have potential to reduce transport-related CO_2 emissions, diesel engines emit more particulates[4]. Diesel encompasses adverse health effects, not health co-benefits. Improvements in diesel engines in Europe resulted in stable, but not lower particulate level.

Health benefits related to a reduction in noise pollution

Physiological responses of traffic-related noise include rises in stress levels and blood pressure. High traffic-related noise levels are associated with cardiovascular diseases[4,13] and sleep disturbance[4,13], imposing increased risk for mental ilness[4,13].Low carbon transportation polices linked to traffic-related noise reduction, include transport and land use polices that reduce traffic speed and volume. Specific road materials also play a role. Porous asphalt can reduce noise level, equivalent to almost halving the volume of traffic[15]

Health benefits related to a reduction in road traffic injuries

Road traffic injuries is a largely predictable and preventable risk that lead the top risks factors for the burden of disease in Latin America[16]. Walkers, cyclists and motorcyclists are more vulnerable. In São Paulo and Valledupar, traffic-related injuries were more severe among motorcyclists.

Low carbon transportation polices that reduce the risk of traffic-related injuries include safe networks for active transport and reduced traffic speed,[4,13,15]. After two months, a 20 km/h reduction in the limit speed for cars in a major road in São Paulo, reduced deaths and injuries in 36%, with gains in traffic congestions. Rail systems also seems to

pose lower risk for road traffic injuries[4,15].

Health benefits related to an improvement in physical activity levels

Physical inactivity is the fourth leading cause of death worldwide[16] and figures among the top ten risk factors for the burden of disease in Latin America and Caribbean[17]. Physical inactivity is one of the factors driving the global increases (in developing world inclusive) in cardiovascular disease, type 2 diabetes, overweight, obesity and some types of cancer (colon and breast)[4,13,15-18]. More physical activity is related to less depression, anxiety and osteoporosis[4,13]. In São Paulo, the proportion of children traveling to school by active transportation deceased nearly 10% between 1997 and 2007, whereas the proportion of children traveling by private car increased in similar rates[19]. While the time spent in trips to school nearly double in the period for those travelling by car, mean time duration of active transport trips to schools remained unchanged in the period[19].

The major low carbon transportation police that increase physical activity levels is active transportation alone or as part of a journey[4]. Each additional kilometre walked per day reduces in 4.8% the risk of obesity[18]. Outdoor physical activity promoted by active transportation seems to encompass even more benefits for mental health[4,13]. Outdoor exertion promotes exposure to sunlight, increasing vitamin D levels[4], but also the risk for skin cancer in tropical Latin American cities. Specific orientations for sunlight protection during the day might be necessary in Latin America. A recent review[20] concluded that the health gains of active transportation outweigh the risks imposed by traffic accidents and exposure to air pollution.

Low carbon transportation polices encompasses economic and social gains

Long journeys reduce the time for leisure, rest and work with health, social and economic consequences. Low income adolescents spent more time during journeys, because they usually live far from their jobs and have less access to public transportation. The consequent fewer time for study decrease their future job opportunities, reinforcing social inequalities. Improving mobility by public transport among groups with less access to private vehicles (women, children, elderly, people with disabilities and lower income groups) enhances access to economic and social

opportunities, promoting equity[4].

The cost of immobility in São Paulo was estimated in 1% of the Brazilian gross domestic product. A combination of BRT and active transportation infrastructure improvements in Latin America could reduce GHG emissions by 25%, at a cost of US30 per tonne of CO_2 reduction[4].The potential reduction in local pollutant levels from a reduction in GHG emissions, already discussed, can be even greater if long-range transport of air pollutants, long demographic changes and the influence of climate change or air quality are taken in account.

Latin America can widely benefit from low carbon transportation polices

The links between transportation and health are wide and well documented[4,13-15], butthere remains some distance between theory and practice[14]. Low carbon transportation polices reduces GHG emissions and local pollutants, while encompasses local and immediate health benefits. The international scenario of global climate chance agreements[1,4]favour the adoption of more sustainable transportation modes, particularly in Latin America, where the transport sector leads CO_2 emission from fossil fuel combustion[2].Implementation might be cost effective. Latin America is a highly urbanized continent (80% of its population live in cities), where many cities combine elevated levels of air pollutants, large numbers of exposed people and relatively less stringent emissions standards for the transport sector, enhancing the health benefits of low carbon transportation polices. Transportation polices should be considered an environmental and a health police.

Highlights

Latin America scenario

- Compared to other continents, air quality and GHG emissions figure in an intermediary scenario in Latin America and there is room for improvements.
- The transport sector leads the CO_2 emission from fossil fuel combustion in the region.
- Low carbon transportation polices encompasses local and immediate health benefits due to reductions in noise and air pollution levels, improvements in physical activity

levels, among others.

- Inefficient fossil fuel combustion results in higher air pollution levels in developing economies (including Latin American cities), compared to developed economies.
- More efficient combustion technologies that release less particulate pollution per CO_2 emission are already used in developed economies and could be adopted to reduce the burden of air pollution in developing economies (in Latin American cities inclusive).
- As a highly urbanized region, a large number of people are exposed to air pollutants in the continent and its related health risks.
- Better air quality would improve the health of Latin American populations.
- More than an urban planning instrument, transportation polices should also be consider an environmental and a health police.

Figure 1.Global energetic inefficiency index. The index compares the ratio of PM_{10}/CO_2 among countries in 2010 to its correspondent development status. PM_{10} and CO_2 data from the World Bank[8,9]. Human Development index data from the United Nations[10]

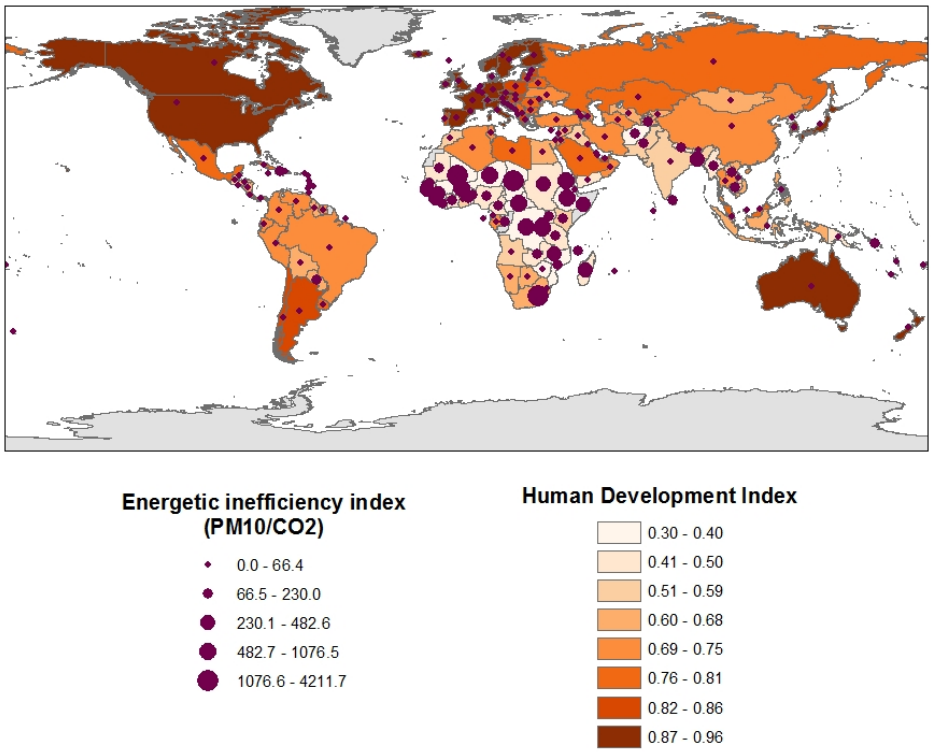
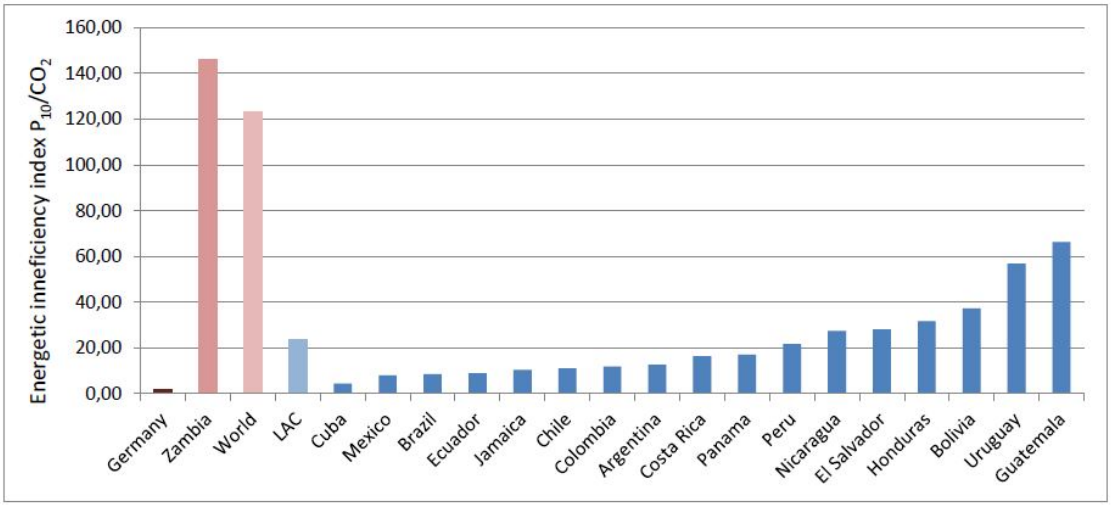


Figure 2. Energetic inefficiency index in selected Latin American and Caribbean countries. The graphic compares the energetic inefficiency index (PM_{10}/CO_2) in 2010 in Latin American and Caribbean countries to selected high and low income countries and to the world mean. PM_{10} and CO_2 data from the World Bank[8,9]. LAC represents the mean value of the index for Latin American and Caribbean countries.



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4.2. Estudo na ausência de dados secundários sistematizados

Durante a condução do estudo sobre poluição e câncer, descrito anteriormente, notei que, de modo geral, os países em desenvolvimento tinham poucos ou não tinham estudos sobre poluição do ar e saúde. Uma das possíveis e frequentes explicações é a falta de dados locais de qualidade sobre a exposição, o que também indica ausência de condições básicas para o controle da qualidade do ar. De fato, ao contrário da maioria dos países desenvolvidos, muitos países em desenvolvimento não oferecem plataformas de livre acesso para os dados de exposição, ou não as disponibiliza de uma forma amigável, o que não necessariamente significa que não esses países dispõe de nenhum tipo de dado de monitoramento local. Como resultado, regiões em desenvolvimento são pouco representadas nas análises globais sobre poluição do ar e saúde. Sendo assim, buscamos informações sobre a cobertura do monitoramento local da poluição do ar na África, América do Sul e Oriente Médio em agências nacionais e internacionais e na literatura científica. Mesmo na escassez de dados públicos secundários sistematizados, construímos uma narrativa mostrando com números a cobertura do monitoramento da poluição do ar em países em desenvolvimento, diferenciando a completa ausência de dados da falta de dados sistematizados. Apesar de exclusivamente descritivo, o estudo recebeu o prêmio "*New Voices in Global Health* 2014", uma competição de resumos com o intuito de destacar pesquisas e inciativas de futuros líderes em saúde global e foi publicado no *The Lancet*[57]. Vide a seguir o resumo na íntegra.

Air monitoring coverage in low-income countries: an observational study

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Abstract

Background Outdoor air pollution is among the top ten risk factors for disease and is carcinogenic for human beings. Monitoring air pollution is a fundamental requirement to implement policies to improve air quality and allow scientists to more precisely quantify the risks of air pollution exposure. We assessed the coverage of air pollution monitoring in several regions.

Methods We did this observational study for Africa, Middle East and South America. We searched information about air quality monitoring coverage from international and national agencies (including WHO, World Bank, and national environmental protection agencies) and in previous scientific studies. We classified monitoring coverage as (1) campaigns (measurements reported in scientific publications with up to 1 year of temporal coverage or by WHO without temporal coverage reported), (2) one station (one fixed station with yearly coverage), or (3) network (more than one station with yearly coverage).

Findings In Africa, air pollution monitoring information was unavailable for 66% of countries, none was available from one station, 14% was from campaigns, and 20% from networks. In Middle East, 28% of countries had no monitoring information, 44% was from campaigns, and 28% was from networks, with none from one station. In South America, 31% of countries have no monitoring information and 69% had information from networks, with none from campaigns or one station.

Interpretation Information about air pollution concentrations is scarce in low-income countries. Air quality is unlikely to improve in countries where data are scarce. These data are paramount to manage air pollution and to estimate the risks to which populations are exposed.

Funding São Paulo Research Foundation.

Contributors

LF and PS designed the study. LF and MVeras collected data. LF, MV, and LVB analysed data. LF, MV, LVB, and PS interpreted data. LF, LVB, and PS wrote the abstract.

Declaration of interests

We declare no competing interests.

4.3. Estudo a partir de revisão sistemática e metanálise

Conduzi uma revisão sistemática e metánalise sobre os efeitos de curto prazo do material particulado e construí a narrativa a partir da América Latina. Os resultados para o $MP_{2.5}$* já foram finalizados e estão em processo de submissão (vide manuscrito a seguir). A coordenação do Capítulo Latino Americano da Sociedade Internacional de Epidemiologia Ambiental se interessou pelo estudo e solicitou-me que eu o apresentasse na reunião do capítulo que ocorrerá este ano (2016) durante a conferência anual da sociedade.

* $MP_{2.5}$ refere-se ao material particulado com diâmetro menor que 2.5 micrometros

Artigo em processo de submissão.

O material suplementar referente a este artigo está apresentado na seção de Anexos (Anexo B).

Short-term effects of $PM_{2.5}$ on daily health events in Latin America: a systematic review and meta-analysis.

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Acknowledgments: we thank the librarian assistants Mabel Fernandes Figueiredo and Rosa Fischi for assisting with the search strategy and retrieving references. We did not receive specific financial support to conduct this systematic review.

Abstract

Background: Short-term exposure to $PM_{2.5}$ is consistent associated with increased risk for morbidity and mortality, but evidence for Latin American population is scarce.

Objective: Summarize the effect of short-term exposure to $PM_{2.5}$ on morbidity and mortality in Latin American and evaluate evidence coverage and quality in the continent, using systematic review and meta-analysis.

Data sources and extraction: The comprehensive search (six online databases and the reference lists of relevant studies) identified time-series or case-cross over studies investigating the sort-term associations between $PM_{2.5}$ and daily health events (mortality, hospitalizations and emergency room visits for all-natural, cardiovascular or respiratory causes) in Latin America. Two reviewers independently accessed the internal validity of the studies and used random-effect models in the meta-analysis.

Data synthesis: We retrieved 1628 studies and elected nine (seven for the quantitative analyses). Each 10μg/m^3 increments in daily $PM_{2.5}$ concentrations was significant associated with increased risk for respiratory and cardiovascular mortality in all-ages (polled RR=1.02, 95%CI, 1.02-1.02 and RR=1.01, 95%CI, 1.01-1.02, respectively). Risks for total mortality in all-ages and elderly, and respiratory hospitalization in children were not significant. Evidence was concentrated in six cities and 33% presented high risk of bias. None of the studies investigated emergency room visits.

Conclusion: Short-term exposure to $PM_{2.5}$ in Latin America is significant associated with increased risk for respiratory and cardiovascular mortality. Evidence is scarce, concentrated in few cities and some presented high risk of bias. Internal validity of epidemiological time-series studies on Environmental Health needs further investigation.

Introduction

Epidemiological evidence of the effects of fine particulate matter [PM with aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$)] on morbidity and mortality is consistent, particularly on cardiovascular and respiratory systems (Anderson et al. 2004; Pope et a. 2006). Biological evidence supporting plausible mechanisms is clear and includes pulmonary oxidative stress, inflammation and altered cardiac autonomic function (Pope

et al. 2006). However, evidence in Latin American is scarce and Systematic Reviews and Meta-analysis (SRMA) on the effects of $PM_{2.5}$ on daily health events rarely pool evidence from Latin America (Adar et al. 2014; Shah et al. 2015). The World Health Organization (WHO) is updating current ambient Air Quality Guidelines, which stablishes standards for pollutants at concentrations considered sufficiently safe for human health (World Health Organization 2015). Transferability of existing concentration response functions (CRF) developed for European and North American cities to other countries with significant differences in air pollution levels are been questioned. According to the experts consulted by WHO, re-evaluation of the existing CRFs for $PM_{2.5}$ is necessary, given the observed changes in the risk at extreme concentrations (World Health Organization 2015). Experts also underscored that current evidence show association of short-term $PM_{2.5}$ exposure with mortality at levels below the current guideline, among other new evidence that need to be evaluated (World Health Organization 2015).

When the WHO air quality guidelines were last updated in 2005 (World Health Organization 2006), monitoring systems were scarce in cities from developing nations, including Latin American cities. Most of the data available in developing regions were exclusively for total suspended particles (TSP) concentrations, an overcome measure of particulate air pollution that includes particulates of bigger size. After a decade, evidence in Latin America remains delayed compared to North America and Europe. While developed countries are concerned with the health effects of fine ($PM_{2.5}$), ultrafine and coarse [PM with aerodynamic diameter 10-2.5 ($PM_{10-2.5}$)] particles, few cities in Latin America depict evidence for these pollutants. Only eight Latin American countries have set National Air Quality Standards for $PM_{2.5}$ (Green and Sánchez 2012),

all above the final target of 25μg/m^3 for 24-hour average, current suggested by WHO (World Health Organization 2006). In 2012, the ESCALA multi-city study has established methodologic foundation for future research in Latin America and provided high quality evidence from nine cities to support air pollution control policies in the region (Romieu et al. 2012). However, the evidence was limited to the effects of PM_{10} on mortality.

Given the very high levels of $PM_{2.5}$ pollution in Africa, Asia and Middle East (Brauer et al. 2012), air pollution in Latin America receives less attention in global analysis. However, between 1990 and 2013, $PM_{2.5}$ annual mean levels trends increased in parts of South America and decreased in parts of Southeast Asia (Brauer et al. 2012).

In this systematic review, we aimed to summarize the evidence of the short-term effects of $PM_{2.5}$ on daily health events in Latin America populations. We also aimed to identify the Latin American cities covered with local evidence on short-term health effects of $PM_{2.5}$ and to evaluate the quality of the evidence identified.

Methods

This study followed a protocol previously registered at PROSPERO (registration CRD42015029673) and is reported according to both: PRISMA Statement recommendations for transparent reporting of systematic reviews (Moher et al. 2009) and MOOSE Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies (Stroup 2000).

Search strategy and eligibility criteria

We searched six online databases (PubMed, Embase, Scopus, Web of Science, Cochrane and Lilacs) up to September 2015 to identify studies conducted in Latin America that analysed the associations of short-term exposure to $PM_{2.5}$ with daily health

events (mortality, hospital admission and emergency room visits). Search combined terms for exposure (e.g. “air pollution”, or “particulate matter”), outcome (e.g. “hospital admission”) and population (e.g. “Latin America” or name of countries). Controlled vocabulary of databases was included in the search string. We did not impose language or date restrictions to the search. We searched the reference lists of relevant reviews and studies for additional manuscripts and used Mendeley software for uploading the references. For detailed search strategy, see the Supplemental Material, S1.

Eligibility criteria included:

a) Original published time-series or case-cross over studies with a minimum period evaluated of one uninterrupted year, conducted in Latin American,

c) Studies that reported quantitative measurements of daily short-term exposure (up to a lag of seven days) to ambient $PM_{2.5}$,

d) Studies that reported daily emergency room visits, hospital admissions, and/or mortality for all natural causes and/or all or selected respiratory causes and or all or cardiovascular causes. Related International Code of Disease (ICD 9th and 10th revision) for the causes included were: ICD-9 001–799, ICD-10 A00-T98 and Z00-Z99 (all natural causes), ICD-9 460-519, ICD-10 J00-J99 (respiratory causes) and, ICD-9 390-459, ICD-10 I00-I99 (cardiovascular cases).

e) Studies that calculated or provided enough information to estimate the relative risk of the daily health event associated with an increment of $10\mu g/m^3$ in $PM_{2.5}$ levels.

f) Studies that reported the risk exclusively by subgroups other than age, daily event or diseases groups of interest for this review (e.g. by season or chemical composition of the particle) were excluded.

Study selection

First, two independent reviewers screened all abstracts and titles for studies that potentially met the inclusion criteria. Then, reviewers evaluated full studies for final inclusion in the SR (Systematic Review) and recorded reasons for exclusion (see the Supplemental Material, Part2). Similar to reviews on global (Atkinson et al. 2014) and European evidence (Anderson et al. 2004), we selected only one study by setting to avoid overlapping of populations (see protocol at PROSPERO, registration CRD42015029673). We solved disagreements between reviewers by consensus along the stages.

Data collection process and items

Data items included citation information (e.g. year of publication) and characteristics of the location (eg. main air pollution sources), population (e.g. age), exposure (e.g. $PM_{2.5}$ levels) and outcomes (e.g. total number of events) (See Table 1). We also collected information necessary to conduct meta-analysis of the relative risks related with $10\mu g/m^3$ increments in $PM_{2.5}$ levels (e.g. association measurements and its 95% Confidence Interval (CI)) and methodological characteristics necessary to assess the quality of the included studies (see Table 2). One reviewer extracted the data into Microsoft Excel 2013 and a second reviewer confirmed the information. Disagreements were solved by discussion.

Risk of bias in individual studies

Since there is no specific tool to evaluate methodological quality of time-series and case cross-over studies, two independently reviewers conducted a qualitative assessment, which classified studies as high or low risk of bias, according to criteria previously registered at the protocol of this study. We also verified funding sources and the conflicts of interest reported, which are recently being considered potential source of

bias (Lam et al. 2014).

Summary measures

We calculated summary effects associated with $PM_{2.5}$ levels in the statistical software RevMan 5.1 by daily event type (emergency room visits, hospital admissions and mortality), cause (total non-external causes, respiratory and cardiovascular causes) and age group (all-ages, elderly and children), if at least two association measurements were available from two different studies. Given that we calculated a polled effect for an entire continent, variations regarding population, outcomes and exposure characteristics among the cities included in the quantitative analysis were expected. For this reason, we used random effects model to estimate the summary measures and present them as Relative Risk (RR) with a 95% Confidence Interval (95% CI) for each increment of $10\mu g/m^3$ in $PM_{2.5}$ 24-hour average levels.

The lag (number of days between the exposure and the health event) reported by studies varied greatly and it was not possible to group the studies by lag structure. The lag used to calculate the summary measure was the lag reported. We chose the lag with the highest effect, if more than one lag was reported.

We used Cochrane Q test (significance level: 0.1) and I^2 statistic to test statistical heterogeneity. I^2 statistic quantifies heterogeneity by calculating the proportion of variation occurred by heterogeneity rather than by chance (Higgins et al. 2003). For I^2, we considered that values ranging from 0 to 30, 30 to 50 and > 50 indicated low, moderate and high heterogeneity, respectively. We also reduced potential heterogeneity due to populations and outcome cause differences by polling evidence grouped by cause/age pairs. We planned to performed sub-groups analysis by pollutant model (single vs multi-pollutant), pollution source (rural vs urban) and risk of bias between

studies (combining low risk of bias studies only), if heterogeneity was statistically significant. Non-quantitative data was presented descriptively.

Publication bias assessment

If 10 or more studies are included in the review we accessed publication bias through funnel plot and Egger test (Egger et al. 1997).

Results

Study selection

Search retrieved 1628 studies, nine were elected for the qualitative analysis and seven for the quantitative analyses (Figure 1). Elected studies were conducted in three countries (Chile, Brazil and Mexico), distributed in six cities, mostly with less than a million inhabitants. None of the studies investigated the effects of $PM_{2.5}$ on emergency room visits.

Automotive was the main source of air pollution reported, followed by biomass burning and industrial sources. $PM_{2.5}$ daily mean varied from 7.5 to 81.0μg/m^3 among the included studies (Table 1).

The most studied decade was the 2000's (44%), followed by the 1990's (35%), 2010's (23%) and 1980's (5%). All elected studies were time-series studies published as articles. Only one was a multi-city study (evaluated the metropolitan area). Elected studies were mostly published in English (89%), and 56% of the included studies used single-pollutant models exclusively (see Supplemental Material, TableS1).

The quality assessment revealed that 33% of the included studies presented high risk of bias, 43% if we consider only studies elected for the quantitative analysis. Frailties in statistical adjustments (e.g. not using the Akaike criteria), in exposure characterization (not using monitoring networks) and controlling for confounders (not controlling for

short trends such as for day of the week) were the main reasons why studies were classified as high risk of bias. When reported, conflict of interest was absent and financial sources were related to governmental agencies and University-related grants (Table 2).

Measurements combined for meta-analysis were derived from single-pollutant models, except for total mortality in elderly, where evidence was available for single and multi-pollutant models. All meta-analysis combined evidence from two different studies, except from hospital admissions where evidence from three were combined. Given the low number of studies combined and their characteristics, we did not perform subgroup analysis by pollution source (rural vs urban) and risk of bias (low vs high risk of bias).

Mortality

Meta-analysis of the risks for respiratory mortality in all-ages associated with $PM_{2.5}$ levels showed a significant 2% increased risk (RR *per* 10µg/m^3 = 1.02, 95% CI, 1.02-1.02; I^2 = 0%) (Figure 2). Meta-analysis of the risk for cardiovascular mortality associated with $PM_{2.5}$ levels showed a significant 1% increased risk (RR *per* 10µg/m^3 = 1.01, 95% CI, 1.01-1.02; I^2 = 0%) (Figure 2). One of the studies combined presented high risk of bias.

Risk for total mortality was not significant neither for all-ages (RR *per* 10µg/m^3 = 1.01, 95%CI, 1.00-1.01; I^2 = 0%) (Figure 2), nor for elderly (RR *per* 10µg/m^3 = 1.01, 95%CI, 1.00-1.02; I^2 = 55%) The risk for total mortality in elderly remained not significant when we combined measures based on multi-pollutant models, all adjusted for O_3: RR *per* 10µg/m^3 = 1.01, 95% CI, 0.99-1.03; I^2 = 73% (see Supplemental Material, Figure S1). All studies combined presented low risk of bias.

For hospital admissions, meta-analysis showed no statistical association between $PM_{2.5}$

levels and daily hospital admissions and presented significant high heterogeneity: RR *per* 10μg/m^3 = 1.03, 95% CI, 0.99-1.08; I^2 = 68%) (Figure 3). The studies combined used satellite-derived measurements and two depicted high risk of bias.

Discussion

Our results showed significant associations between short-term exposure to $PM_{2.5}$ in Latin America and increased risk for respiratory and cardiovascular mortality in all-ages. The risks for each 10μg/m^3 increment in $PM_{2.5}$ levels ranged between 1 and 2% and heterogeneity between studies was low. On the other hand, risks associated with short-term exposure to $PM_{2.5}$ for total mortality in all-ages and in elderly and respiratory hospitalization in children were not significant. Imprecision might explain why some meta-analysis were not statistically significant in our review, since CIs of the combined studies tended to be larger in the non-significant meta-analysis (particularly for hospitalizations meta-analysis), compared to significant meta-analysis (respiratory and cardiovascular mortality). Frequently, multi-city studies find larger effects when the analysis is restricted to elderly populations (Romieu et al. 2012), because elderly are more vulnerable to air pollution adverse health effects. However our meta-analysis for total mortality in elderly was not significant. Because populations are exposed to a complex mixture of air pollutants, not single pollutants, researchers (and policy makers) have being encouraged to move towards a multi-pollutant approach to air quality, rather than single-pollutant models (Dominici et al. 2012). In our review, most of the risks reported were based on single pollutant models. Meta-analysis for multi-pollutant models (adjusted for O_3) were just feasible for total mortality in elderly, but the related risks were not significant in both pollutant models

Our results are partially in accordance with other meta-analysis on the short-term association of $PM_{2.5}$ and daily health events in the world (Adar et al. 2014; Atkinson et

al. 2014), pointing out that, while local evidence is scarce, extrapolating evidence from other regions to control particulate pollution in Latin America might be reasonable.

Compared to the present review, Atkinson et al. (2014) study identified fewer Latin American studies and did not evaluated all the outcomes considered in this review for Latin American region, possible due to differences in the search strategy adopted. We searched Lilacs, a specific database for scientific literature of Latin American, and other databases up to September 2015, while Atkinson's review searched global databases exclusively up to May 2011. While our results are mostly in accordance with Atkinson's global findings, our results contrast with Atkinson's findings for Latin America for total, respiratory and cardiovascular mortality in all-ages. Both reviews combined evidence from two studies to perform meta-analysis, but in our review CIs of the included studies were more precise.

Evidence on the short-term effects of $PM_{2.5}$ in daily health events conducted in Latin America is scarce, concentrated in few locations and publication trend is not increasing. The scarcity of studies in the continent might be reflecting lack of exposure data, since only half of Latin American cities with monitoring stations for $PM_{10,}$ also monitors $PM_{2.5}$ (Green and Sánchez 2012). Moreover, in some cities, $PM_{2.5}$ measurements started in recent years and occur in a few percentage of the existing monitoring stations (MMA 2014). In our review, all Brazilians studies included estimated population exposure through satellite estimations. Sophisticated satellite-based estimates are a promising tool to overcome the scarcity of exposure data, given that correlation with ground-level $PM_{2.5}$ mass might reach 81% (Van Donkelaar et al. 2016) and The Global Burden of Disease Study is already using satellite based $PM_{2.5}$ estimates (Brauer et al. 2012).

One of the strengths of our review was to evaluate the internal validity of the included

studies, which is not frequent in most SRMAs of epidemiological time-series studies, since, to our knowledge, no validated tool evaluates methodological quality of time-series. Despite advances in methodology of SRMAs involving epidemiological observational studies in general (Stroup 2000) and of epidemiological studies of environmental health (EH) in particular (Sheehan and Lam 2015), it is still difficult to adapt the recommendations to assess the risk of bias in time-series studies. Cochrane Collaboration recommend tools for randomized controlled trials and non-randomized studies of intervention (Higgins and Green 2011), both not applicable to time-series design. Yet, time-series studies have being playing a relevant role in air pollution regulatory process, because they estimate the burden of disease attributable to air pollution exposure and the related CRF can be used in cost-benefit analysis (Bell et al. 2004). Time-series studies use regression models to assess the effects of short-term changes in $PM_{2.5}$ levels on acute health effects by estimating associations between day-to-day variations in both air pollution and in mortality and morbidity counts. The study design uses aggregated level data for exposure and outcome. Confounding bias arise from factors that vary in short time scales and may be associated with particulate and health (e.g. temperature). Statistical specificities (e.g. accounting for serial correlation in the residuals) also play a role (Bell et al. 2004).

Our quality assessment followed an *a priori* criteria and two reviewers independently assessed key methodologically potential sources of bias in human epidemiological observational studies in EH in general (e.g. exposure characterization and controlling for confounders) (Sheehan and Lam 2015) and of time-series design in particular (e.g. statistical adjustments) (Bell et al. 2004). Frailties in at least one of the potential source of bias domains were frequent; underlining that internal validity of time-series study

design on EH SRMAs needs further investigations.

Since we retrieved less than 10 studies for each health endpoints (outcome/cause/age), we did not evaluate publication bias, a limitation of this review.

Multi-city studies standardize statistical approach and therefore minimize potential risk of bias due differences in statistical methodology of time-series studies (Bell et al., 2004). To the extent that time-series design usually uses secondary dada relatively accessible from public sources, efforts to conduct high quality multi-city studies might be preferable than conducting meta-analysis based on individual studies data retrieved in a SR. However, $PM_{2.5}$ monitoring stations are scarce in Latin America (Green and Sánchez 2012) and the multi-city study for Latin America region (Romieu et al. 2012) did not evaluate the effects of $PM_{2.5}$ on health, making this review relevant.

Conclusion

Evidence in Latin America is scarce, concentrated and trend of publication is not increasing. Short-term exposure to $PM_{2.5}$ in the continent is significant associated with increased risk for respiratory and cardiovascular mortality in all-ages in region. Our results are in accordance with evidence from other parts of the world, pointing out that, while local evidence is scarce, extrapolating evidence from other regions to control particulate pollution in Latin America might be reasonable. Quality assessment identified frailties in key methodological sources of bias in observational studies in EH in general (exposure characterization and controlling for confounders) and in time-series design in particular (statistical adjustments), thus assessing the internal validity of time-series study design in SRMA on EH needs further investigations.

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Table 1. Characteristics of the studies included in the systematic review

Reference	Study period	City (Country)	Air pollution sources†	Inhabitants reported*	$PM_{2.5}$ mean (SD) in µg/m^3	Population in years	Outcome (cause)	Number of events	Pollutant model	Risk of bias
Dales et al. 2010‡	1998-2005	Santiago metropolitan region (Chile)	NI	5.370.000	32.9 (20.2)	All-ages	HA(CV°)	282.645	both	low
Cesar et al. 2013	2011-2012	Piracicaba (Brazil)	biomass, automotive	350.000	26.8 (16.7)	<10	HA(R)	437	single	high
Ignotti et al. 2010	2000-2004	Alta Floresta (Brazil)	biomass	101.278	20.4 (32.6)	<5	HA(R)	481	single	high
Silva et al. 2013	2005	Cuiabá (Brazil)	biomass	550.562	7.5 (10.4)	<5	HA(R)	1.152	single	low
Loomis et al. 2009‡	1993-1995	Ciudad de México (Mexico)	automotive, industrial	2.500.000	27.4(10.5)	<1	M(A)	2.798	both	low
Borja-Aburto et al. 1998	1993-1995	Ciudad de México (Mexico)	automotive, industrial	2.500.000	27.0 (11.0)	All-ages, >65	M(A,R,CV)	1.152	both	low
Sanhueza, et a. 1998	1988-1993	Santiago (Chile)	NI	NI	81.0 (NI)	All-ages, >65	M(A)	76.442 (A,>65)	both	low
Valdes et al. 2012	1998-2007	Santiago (Chile)	NI	NI	34.0 (NI)	All-ages	M(R,CV)	92.891	single	high
Reyna et al. 2012	2003-2007	Mexicali (Mexico)	automotive, unpaved roads	856.000	60.6 (32.3)	All-ages	M(A*)	872.350	single	low

Abbreviations: SD, standard deviation; NI, not informed; PM, particulate matter; M, mortality; HA, hospital admissions; E, emergency room visits; A, all non-external causes; CV, cardiovascular disease; R, respiratory disease; Single, single-pollutant model; Multi, multi-pollutant model; Both, single and multi-pollutant model. * Not all studies evaluated the whole population of the city investigated, therefore some inhabitants reported reflect the population of the area covered by the hospitals included in the analysis, not all the city. *Reyna et al. (2012) also evaluated respiratory mortality, but did not present the associations with short-term exposure to $PM_{2.5}$ for this outcome. °Study evaluated specific cardiovascular disease: I26 an I80 according to the International Classification of Disease, 10th Revision (ICD-10). ‡not included in the quantitative analysis. Dales et al. (2010) was the only study that evaluated cardiovascular hospitalizations and Loomis et al. (1999) the only study that evaluated mortality in children.

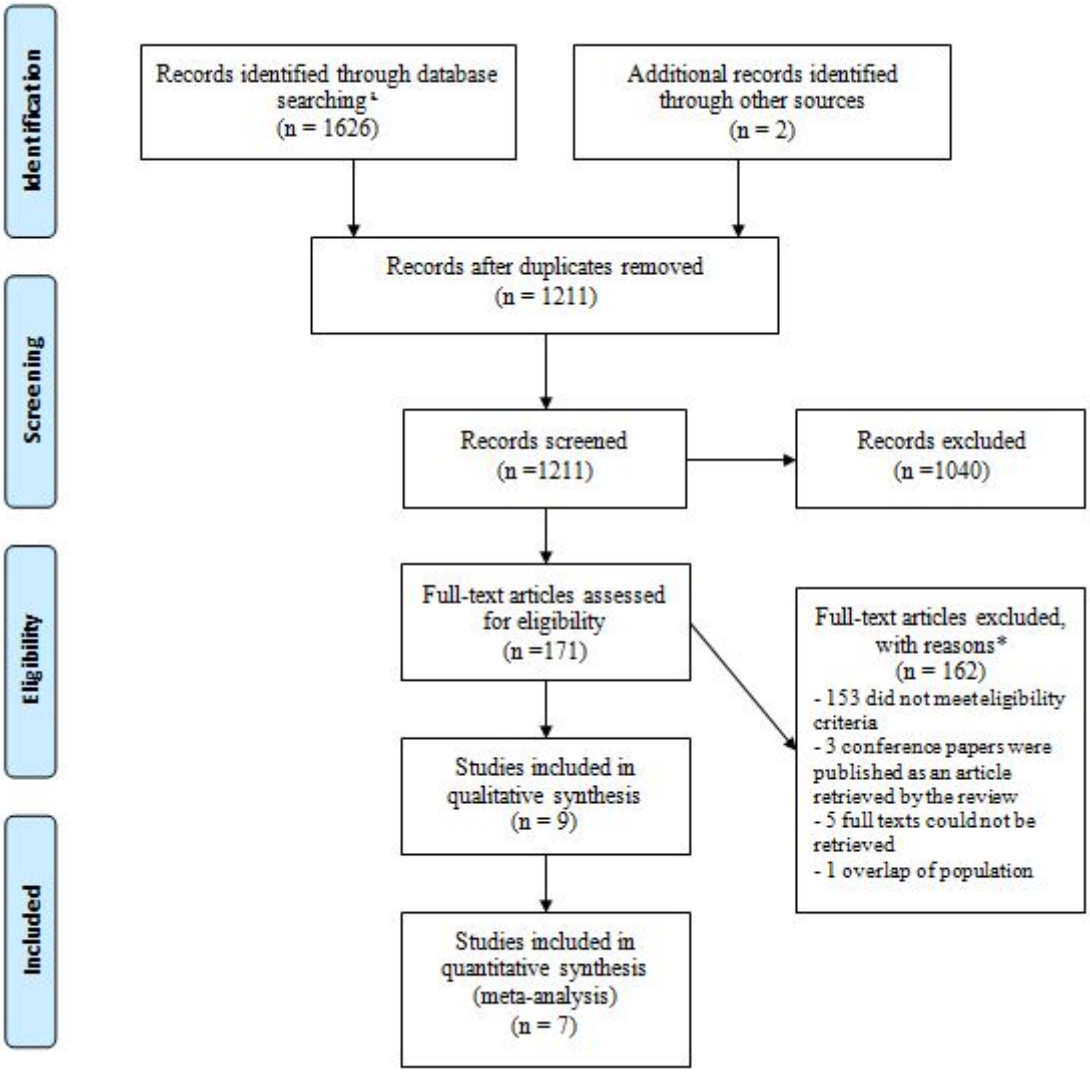
Table 2. Quality assessment of the included studies in the systematic review

Reference	Selection		Exposure			Confounders				Statistical adjustments of the model			Founding source	Conflict of interest
	ICD	Source[◊]	Source[◊◊]	Network	Daily	Long trends	Short trends	Temp	Hum	Autocorrelation	Akaike	Risk of bias		
Borja-Arbuto et al., 1998	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Low	NI	NI
Loomis et al. 1999[‡]	Y	Y	Y	N	Y	Y	N	Y	N	Y	Y	Low	NI	No conflict
Cesar et al., 2013	Y	Y	Y	N*	Y	N	N	Y	N	N	N	High	Governmental research agency	No conflict
Dales et al., 2010[‡]	Y	Y	N	Y	Y	N	N	Y	Y	Y	Y	Low	NI	No conflict
Ignotti et al., 2010	Y	Y	Y	N*	Y	N	N	Y	Y	N	N	High	Governmental research agencies	NI
Reyna et al., 2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Low	University-related grants	NI
Sanhueza, et a. 1998	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Low	Governmental research agency and University-related grants	NI
Silva et al. 2013	Y	Y	Y	N*	Y	Y	Y	Y	Y	N	N	Low	NI	No conflict
Valdes et al., 2012	Y	Y	Y	N	N	Y	Y	Y	Y	N	N	High	NI	No conflict

Abbreviations: ICD, International Code of Disease informed; Y, yes; N, no; U, unclear; NI, not informed; Network, monitoring network; Daily, Daily Measurements; Akaike, Akaike criteria; Temp, temperature; Hum, humidity

† Studies included in the quantitative analysis. N*, satellite; [◊]Source of the outcome data; [◊◊]Source of the exposure data; [‡]not included in the quantitative analysis. Dales et al. (2010) was the only study that evaluated cardiovascular hospitalizations and Loomis et al. (1999) the only study that evaluated mortality in children.

Figure 1. Study selection flow diagram

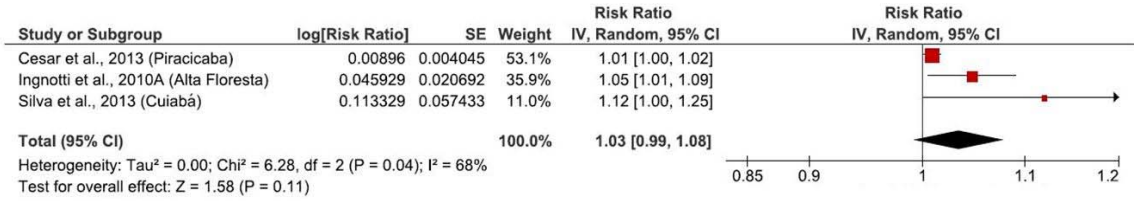


* see the Supplemental Material, Part2 for the complete list of studies excluded by reason.
Ł databases searched: PubMed, Embase, Scopus, Web of Science, Cochrane and Lilacs up to September 2015

Figure 2. Forest plots for the risks for daily mortality by cause associated with short-term exposure to $PM_{2.5}$ levels.

Risks are reported for increments of $10\mu g/m^3$ in $PM_{2.5}$ levels and were calculated for all-ages, based on single-pollutant models. (a) all-causes, (b) respiratory causes, and c) cardiovascular causes.

Figure 3. Forest plots for the risks for daily respiratory hospitalization in children associated with short-term exposure to $PM_{2.5}$ levels by pollutant model.



Risks are reported for increments of $10\mu g/m^3$ in $PM_{2.5}$ levels and were calculated based on single-pollutant models.

4.4.Narrativas para públicos diversos

Nesta tipologia, incluo um trabalho sobre poluição do ar e três trabalhos sobre urbanização e qualidade de vida, entre artigos e capítulos de livros focados em públicos diversos. Ir além da poluição do ar e trabalhar com outros temas relativos à urbanização e qualidade de vida são um indicativo de que de fato consegui integrar diferentes áreas do conhecimento.

4.4.1. Capítulo de livro sobre poluição do ar e reprodução humana

Neste estudo[58] contribui como coautora e auxiliei na construção da narrativa do tema, principalmente a partir da escolha e produção de uma imagem para a narrativa do capítulo. De modo similar as imagens selecionadas na tipologia 4.1. Estudos a partir da análise de dados secundários, utilizei dados secundários, neste caso dados globais de fertilidade e poluição do ar. Contribui ainda para a construção da estrutura da narrativa do capítulo, particularmente para as considerações finais. O livro foi publicado em 2015. A seguir apresento o capítulo na íntegra.

Chapter 2
Impacts of Air Pollution on Reproductive Health

Mariana Matera Veras, Natália de Souza Xavier Costa, Laís Fajersztajn, and Paulo Hilário Nascimento Saldiva

2.1 Introduction

Humans are continuously exposed to mixtures of environmental contaminants and a vast body of evidence now link exposure to these chemicals with an increased incidence of reproductive and developmental disorders (Woodruff and Walker 2008; Sadeu et al. 2010).

Since the second half of the twentieth century, the harmful effects of air pollution on human health have been the subject of many studies. Episodes of high levels of air pollution experienced by cities in Europe and the United States have enlightened both government agencies and the global community public about the harmful effects of air pollution on human health. Infamous examples include both the London Fog of 1952 and Donora Smog of 1948 that were associated with significantly elevated rates of hospital admissions and mortality (Logan 1953; Helfand et al. 2001). Similarly the more recent Bophal gas disaster (India, 1984) should also be remembered. In this tragic example, a methyl isocyanate gas leak killed 2,500 people in 5 days and many more were condemned to long-term morbidity including serious reproductive dysfunctions (Sriramachari 2005). Subsequent to these episodes, clean air legislations and other regulatory actions have significantly

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reduced ambient air pollution in many regions of the world, especially in both North America and Europe (Chen et al. 2007). Despite successful regulatory oversight, air pollution in urban centers remains a substantial risk factor to global human health.

The respiratory tract is the first system to be in contact with the air pollutants. Respiratory and cardiovascular diseases are the most commonly observed effects associated with exposure to low levels of air pollution followed by neoplasia (Schwartz 2006; Pope et al. 2009; Dockery 2009). Recent studies support that common environmental air pollutants that we contact in our daily life and to which exposures are unavoidable could also affect both reproductive health and fetal development. Exposure to ambient air pollution appears to adversely impact fertility, pregnancy outcomes, and fetal health and development (Maisonet et al. 2004; Parker and Woodruff 2008).

Epidemiological studies suggest the association between exposures to air pollution and impairment of reproductive health. However, these studies also recognize and acknowledge many uncertainties with regard to this association (Slama et al. 2008), such as few evidence of plausible biological mechanisms, limited information on personal exposures, difficulties in linking particulate matter (PM) composition or single constituent to the biological effects (Pope 2000; Chen et al. 2008; Valavanidis et al. 2008; Ren and Tong 2008). Despite the adoption of different study designs and statistical evaluations and the potential of confounding variables (e.g. maternal smoking, gestational age, and socioeconomic factors), and lack of consistency in findings, these epidemiological investigations suggest a causal association.

Epidemiological studies are important to help guide further investigation. However, many unanswered questions remain with regard to the association between air pollution and reproductive health including;

- What are the mechanisms involved in decreased fertility due to the exposure to increased PM concentration?
- Which trimester of pregnancy is most relevant to the impairment of fetal development?
- Which component of the PM presents a higher risk for reduced birth weight?
- Are the mechanisms involved in decreased male fertility the same as in females?
- Could multigenerational exposure to ambient PM concentration present cumulative effects?

Future studies utilizing animal models and carefully designed human clinical investigation will help address the current gap in knowledge. Toxicological and clinical studies are necessary to confirm associations elucidate mechanisms involved, identify most susceptible subgroups, and to create ways to reduce these impacts on human health.

In this chapter, we will focus on the major epidemiological findings, current experimental evidence, and possible molecular mechanisms involved in the impairment of the reproductive process associated with exposure to common urban air pollution.

2.2 Urban Air Pollution

Air pollution is a widespread environmental contaminant. Expansion of industry and vehicular traffic has had a major impact on the overall air quality in urban areas over the last decades. This contributed to widespread contamination of the environment by thousands of harmful compounds derived from exhaust emissions. In a broad sense, air pollution can be defined as a mixture of gaseous, liquid, and solid substances containing many toxic components which include; CO, NO_2, SO_2, O_3, Pb, polycyclic aromatic hydrocarbons (PAH) and particulate matter (PM) (WHO 2005).

Because of the recognized health impacts, significant efforts have been placed on investigation and regulation of the particulate fraction of air pollution. As defined by Collbeck and Lazaridis (2010), particulate matter (PM) is a complex mixture of solid particles, liquid droplets, and liquid components contained in the solid particles constituted by many different chemical species originating from a wide variety of sources. Particles can be produced by combustion, suspension of soil material, and also from chemical reactions in the atmosphere. Nitrates, sulphates, elemental carbon, organic substances (VOC, PAH), metals (Cd, Pb) and mineral material (Al, SI, Fe and Ca) are major constituents of airborne PM (Colbeck and Lazaridis 2010; Heal et al. 2012). Particle size ranges vary considerably from a few nanometers (nm) to several micrometers (um), which strongly determine particle lifetime in the atmosphere and deposition in the respiratory tract.

The particles are classified according to their aerodynamic diameter, as PM_{10} [particles with an aerodynamic diameter smaller than 10 μm], $PM_{2.5}$ [aerodynamic diameter smaller than 2.5 μm] and $PM_{0.1}$ [aerodynamic diameter smaller than 0.1 μm] (Colbeck and Lazaridis 2010). The size and its composition are directly linked to negative health effects. The observed high toxicity of the smaller size fractions is believed to be due to the fact that they may reach the deeper portion of the lungs and may translocate into the circulation. Further these fractions contain higher concentrations of polycyclic aromatic hydrocarbons (PAH), semiquinones, metals, transition metals, and have a higher radical generating capacity (Squadrito et al. 2001; Kok et al. 2006).

2.3 Epidemiological Findings

The evidence for harmful effects at realistic urban air concentrations of air pollutants predominantly come from epidemiological studies (Slama et al. 2008; Stillerman et al. 2008). In this section, we will present recent reports that indicate that exposures to ambient levels of air pollutants (PM, NO_2 SO_2 and O_3), in addition to the recognized adverse cardio respiratory effect are associated with negative impacts on reproductive health.

Increased risks for low birth weight, prematurity, neonatal and post-neonatal mortality and congenital defects have been reported to be associated with exposures to ambient air pollution. Beyond the recognized adverse consequences on pregnancy outcomes, exposure to air pollution is associated with adverse impact on reproductive function including fertility. Furthermore, studies have shown that periods of elevated air pollution were significantly associated with changes in semen quality and damages in sperm DNA (Dejmek et al. 2000; Rubes et al. 2005).

2.3.1 Fertility and Fecundability

Very few studies have addressed the effects of ambient air pollution on human fertility. Available studies focus on the primarily impact on male fertility, probably due to readily accessible semen acquisition and analysis (Sokol et al. 2006). Detrimental changes in various semen parameters such as motility, sperm morphology, and DNA are reported, which may cause reduced fertility in males or miscarriage in females.

The positive association of the adverse effects of air pollution exposures on pregnancy outcomes has redirected the attention of the researchers to other important aspects of reproductive health including fertility. One of the first studies that investigated the effects of air pollution on fertility was conducted by Djemek et al. (2000). In this study, they have evaluated the impact of SO_2 on fecundability (the probability of conceiving during the menstrual cycle) in the first unprotected menstrual cycle (FUMC) of 2,585 parental pair in a heavily polluted region of Northern Bohemia. They found that adjusted odds ratios of conception in the FUMC may be reduced in couples exposed to mean SO_2 levels >40 pg/m^3 in the second month before conception. In a previous study with the same population, they have also found an association between PM_{10} and reduced conception rates (Dejmek et al. 1998). Slama et al. (2013) reanalyzed the data of the study by Dejmek et al. (2000) and defined the exposure window with respect of the start of the period of unprotected intercourse and considered the impact of $PM_{2.5}$, carcinogenic polycyclic aromatic hydrocarbons (c-PAH), ozone (O_3), nitrogen dioxide (NO_2) levels, in addition to SO_2 on fecundability. Their new results highlight that $PM_{2.5}$ and NO_2 levels in the 2 months before the end of the first month of unprotected intercourse were associated with decreased fecundability. This observation highlights the important concept of lag time between exposure and observed health consequences.

Selevan et al. (2000) showed that elevated period of air pollution were significantly correlated with changes in various semen parameters of young Czech men including; proportionately fewer motile sperm, less sperm with normal morphology or normal head shape, and proportionately more sperm with abnormal chromatin. Based on this preliminary findings, Rubes et al. (2005) monitored semen quality in a cohort of young Teplice residents over longer periods of time (periods of exposure to both low and high air pollution) and found a significant association between exposure to high levels of air pollution and decreased sperm chromatin integrity.

In the United States (Salt Lake City), Hammoud et al. (2010) demonstrated that $PM_{2.5}$ concentration was negatively correlated to sperm motility 2 months and 3 months after exposure, which coincides with the duration of spermatogenesis (72 days). However, a study of Hansen et al. (2010) did not support a consistent pattern of association between O_3 and $PM_{2.5}$. They performed analysis of several measures of semen quality and found only statistically significant adverse association between increased $PM_{2.5}$ averaged over the 0- to 90-day period before semen sampling and an increase in the percentage of sperm with abnormally shaped heads and the percentage of sperm with cytoplasmic droplets. However, after controlling for season and temperature results failed to reach statistical significance.

In the study of Sokol et al. (2006), there was a significant negative correlation between O_3 levels (70–90 days before collection) and average sperm concentration, which was maintained after correction for birth date, age at donation, temperature, and seasonality. These epidemiological results are in line with occupational exposures (De Rosa et al. 2003; Guven et al. 2008) and experimental studies of diesel exhaust inhalation and detrimental effects on sperm (Izawa et al. 2007).

There are very limited studies on the impact of air pollution on female fertility. We are aware of only two studies available in the literature on female fertility that were conducted by Perin et al. (2010a, b). These studies evaluated the impact of PM exposure during the follicular phase of the menstrual cycle or during the preconceptional period of women undergoing IVF/ET on early pregnancy loss and miscarriage. Both studies support an association between brief exposure to high levels of PM and the adverse gestational outcomes. This is an area that would likely benefit from additional studies.

Human fertility is declining in different parts of the world for unclear reasons. There are many hypothesis that have been used to explain this observation. Among the most supported causes of worldwide declining fertility are the delay of childbearing by modern women and other changes in social factors. However, there is also a growing incidence of impaired fecundity among young women and men, which cannot be easily explained by societal factors. Nutritional status, obesity, drugs, smoking habits, stress and increasing exposures to environmental pollutants, such as air pollution, are also plausible factors involved in human reduced fertility that deserve more attention.

2.3.2 Low Vitamin D and Immune System Alterations

Besides the "visible" effects of air pollution on fetal health, there is growing evidence of the impact of maternal exposure to urban air pollution on "non-visible" fetal outcomes. Serum vitamin D levels in the mother and fetus seems to be affected by air pollution. Vitamin D is scarce in natural food and the main source of vitamin D for humans is its synthesis from 7-dehydrocholesterol upon exposure to UVB solar radiation and conversion to circulating metabolite called 25-hydroxyvitamin D [25(OH)D] in the liver. Deficiencies in vitamin D are associated with different

bone diseases and more recently it has been involved in other diseases including cardiovascular (Kim et al. 2008) and autoimmune diseases (Lange et al. 2009).

In general, low intake of vitamin D and insufficient exposure to sunlight constitute the main causes of vitamin D deficiency. However, recent studies point out that exposure to air pollution may also contribute to low serum levels of vitamin D in women and in the unborn child as a consequence of maternal deficiency. In the study conducted by Baïz et al. (2012), maternal exposure to ambient urban levels of NO_2 and PM_{10} during the whole pregnancy was a strong predictor of low vitamin D status in newborns. Moreover, Kelishadi et al. (2013) have also found that air quality had an inverse and independent association with 25(OH)D levels of mothers and their neonates and Hosseinpanah et al. (2010) have shown that deficiency in vitamin D to be prior to pregnancy. In their study, they found that women living in polluted areas present with lower levels of serum 25-OH-D which is comparable to vitamin D deficiency.

Potential mechanisms that could explain this relationship are based on the impact of smoking on vitamin D status (Brot et al. 1999). It has been suggested that changes in inflammatory profile and oxidative stress caused by smoking affects liver function and hence vitamin D synthesis or affecting maternal intestinal absorption of vital vitamins and minerals (Need et al. 2002). Exposure to air pollutants may have similar impact on vitamin D status. Beyond observed differences in vitamin D, exposure to air pollution could result in changes of the immune system including; NK, T lymphocytes, and IgE content of umbilical blood (Herr et al. 2010, 2011). Maternal exposure to air pollution could have lasting effects of either gestational or pre-gestational exposures on their offspring. The consequences for the future health of these individuals remains unknown, but these effects could have far reaching impacts.

2.3.3 Gestational Outcomes

Studies conducted in different continents (Europe, Asia and Americas) consistently report that expectant mothers exposed to air pollution have greater risks of having negative gestational outcomes (Gouveia et al. 2004; Ha et al. 2001; Wang et al. 1997). However, it is not clear from the studies whether the effects are due to a specific pollutant or to the interactions of different pollutants and in which trimester exposures are more detrimental to fetal development. Negative gestational outcomes are predominant reproductive effects associated with exposures to ambient air pollution and are discussed in detail in Chap. 3. In this section, we will briefly highlight the gestational outcomes and its association with criteria pollutants in order to compare with experimental evidence.

The causes of the negative pregnancy outcomes are not well understood but it is clear that these outcomes have multifactorial causes and there are scientific evidence that environmental factor, such as air pollution, can contribute or aggravate these outcomes. Furthermore, there are groups within population that may be more susceptible to air pollution exposure. These groups include individuals with

preexisting circulatory and respiratory conditions and those socially and economically disadvantaged. In general people with low social and economic status live in more polluted areas, lack adequate health care, and spend more time near high traffic roads that may increase exposures to air pollutants and consequently increase the risks of adverse birth outcomes (Woodruff et al. 2003; O'Neill et al. 2003; Ponce et al. 2005; Gilbert et al. 2007; Ono et al. 2013).

2.3.3.1 Low Birth Weight

The prevalence of low birth weight (LBW), as defined by WHO as weight at birth of less than 2,500 g (5.5 lb) is estimated to be 15 % worldwide with a range of 3.3–38 % (http://www.who.int/nutrition/topics/lbw_strategy_background.pdf) and occurs mostly in developing countries; coincidentally these countries has elevated levels of air pollution (http://www.who.int/gho/phe/outdoor_air_pollution/phe_012.jpg). This topic is covered in more detail in Chap. 3.

Birth weight is an important indicator of subsequent health issues; low-birth-weight babies are more prone to develop hypertension, coronary heart disease, and non-insulin-dependent diabetes during adulthood (Osmond and Barker 2000). Evidence from studies conducted in developed and developing countries, China (Wang et al. 1997), Australia (Mannes et al. 2005), Chezec Republic (Dejmek et al. 1999); and USA (Ritz et al. 2000) point out that PM_{10}, $PM_{2.5}$ and SO_2 are the major pollutants associated with increased risks of LBW. However, other studies verified that exposures during pregnancy to CO, O_3, and NO_2 could also be associated with LBW (Morello-Frosch et al. 2010).

2.3.3.2 Preterm Birth, Intrauterine and Neonatal Mortality

Although less frequently reported, intrauterine and neonatal mortality and pre-term birth (PTB) (Glinianaia et al. 2004; Maisonet et al. 2001; Srám et al. 2005) are also outcomes associated with air pollution. Maternal first trimester exposure to ambient air pollutant exposure seems to be the critical period for PTB. However, Huynh et al. (2006) observed no association between PTB and ambient air $PM_{2.5}$ levels near the maternal residence during early pregnancy and late gestation.

In Australia, Hansen et al. (2006) observed that increased levels of O_3, NO_2 and SO_2 during 1st trimester increases the risk of PTB (OR = 1.26, 95 % CI 1.10–1.45). Another study from Korea (Leem et al. 2006) reported that increased levels of CO level during 1st trimester are responsible for the increased risk for PTB [OR = 1.26, 95 % CI 1.11–1.44, p-trend < .001]. Considering traffic proximity, the risk of PTB in Taiwan was elevated among women living close to a major freeway [<0.5 vs. 0.5–1.5 km, OR = 1.30, 95 % CI 1.03–1.65] (Yang et al. 2003). In Los Angeles, Wilhelm and Ritz (2003) found that there was a dose-response relationship between preterm birth and inverse-distance-weighted traffic density among women in their 3rd trimester [OR = 1.15, 95 % CI 1.05–1.26].

2.3.3.3 Fetal Growth and Developmental Abnormalities

Although evidence is less consistent, exposures accrued during gestation and sensitive periods of fetal organ development may be related to developmental abnormalities/congenital defects. Jedrychowski et al. (2004) observed that not only birth weight is affected; changes in other anthropometric measurements were observed, such as reduction in head circumference. Studies conducted by van den Hooven et al. (2012a) using ultrasound measurements observed that NO_2 levels were inversely associated with fetal femur length in the second and third trimester, and both PM_{10} and NO_2 levels both were associated with smaller fetal head circumference in the third trimester. Vrijheid et al. (2011) systematically reviewed epidemiologic studies on ambient air pollution and congenital anomalies and conducted a meta-analysis for a number of air pollutant–anomaly combinations. They conducted meta-analyses for 18 combinations of pollutants and cardiac anomaly groups and found that NO_2 and SO_2 exposures were related to increases in the risk of coarctation of the aorta and tetralogy of Fallot and PM_{10} exposure was related to an increased risk of atrial septal defects.

A large case-control study conducted in California reported a weak association between cleft lip/palate and ambient air O_3 levels near the maternal residence during the second month of gestation. Few studies evaluated if there were associations between maternal exposure to air pollutants and stillbirths. Results from these studies remain inconclusive. Pereira et al. (1998) found an association between daily counts of intrauterine mortality and NO_2, SO_2, and CO concentrations before (≤5 days) delivery. Similarly, Faiz et al. (2013) reported that increased stillbirth is associated with increases in NO_2, SO_2, CO, and $PM_{2.5}$ concentrations in the immediate few days before delivery. In a study by Bobak and Leon (1999) stillbirth rates were not significantly associated with any indicator of air pollution.

2.3.3.4 Preeclampsia

Emerging evidence from a large European study and from three previous studies (Woodruff et al. 2008; Wu et al. 2009; Rudra et al. 2011; Olsson et al. 2013) further indicates that that there is also a positive associations between exposure to air pollution and risks of preeclampsia. However, the studies diverge to in terms of the pollutant associated with preeclampsia. In the largest study conducted in Europe, Olsson et al. (2013) found that exposure to O_3 in the first trimester of gestation are associated with increased risks of preeclampsia. Rudra et al. (2011) found a weak association between CO exposure during the first 7 months of pregnancy (per 0.1 ppm) and preeclampsia (OR = 1.07, 95 %, CI = 1.02–1.13). In another study conducted in the USA, Wu et al. (2009) reported odds ratios of 1.33 (95 %, CI = 1.18–1.49) and 1.42 (95 % CI = 1.26–1.59) for preeclampsia in the highest exposure quartiles for NO_x and $PM_{2.5}$. Increased blood pressure throughout pregnancy has also been observed in mothers who are exposed to air pollution (van den Hooven et al. 2012b; Lee et al. 2013) and both available studies agree that PM_{10} and O_3 are associated to this effect.

2.3.4 Secondary Sex Ratio

In the literature, there are many examples of studies suggesting the impact of both environmental pollution and occupational exposure to certain substances and changes in secondary sex ratio (SSR) (Terrell et al. 2011; Tragaki and Lasaridi 2009; Schnorr et al. 2001). Previous studies have shown changes in sex ratios of populations living near incinerators [lower sex ratio] (Williams et al. 1992) as well as in areas exposed to polluted air from steel foundries (higher sex ratio) (Lloyd et al. 1985). In urban areas with high levels of particulate pollution derived from traffic, there is only one study that investigated if the secondary sex ratio could be affected by air pollution. In this study, Miraglia et al. (2013) have found a significant negative association between SSR and PM_{10} concentration in São Paulo city, Brazil. Although the causality between environmental exposures and declines in secondary sex ration are still controversial, some authors suggest that the SSR as a sentinel indicator of reproductive injury (Davis et al. 1998).

2.3.5 Reproductive System Cancer

Little is known about the role of air pollution in cancers of the reproductive system cancer (e.g. prostate, ovarian and breast cancer). However, an increased risk of lung cancer associated with exposures to outdoor air pollution was consistently observed in studies from Europe, North America, and Asia (Fajersztajn et al. 2013). Thus it is reasonable to suspect that other types of cancer could be caused by long term exposure to air pollutants. The latest IARC release on cancer incidence mortality and prevalence worldwide predict a substantive increase to total 19.3 million new cancer cases per year by 2025, due to growth and ageing of the global population. However, environmental influences and lifestyle factors may also be implicated in this increase; and they highlight the fact that breast cancer incidence has increased by more than 20 %. Vehicular emission is the primary contributor to air pollution in urban areas, its composition include compounds that are recognized as carcinogens, such as diesel exhaust. Recently, the International Agency for Research on Cancer (IARC) of the World Health Organization has classified diesel and gasoline exhaust as carcinogenic to humans as possibly carcinogenic (Loomis et al. 2013).

Few studies have been conducted to evaluate if there is an association between reproductive system cancer and air pollution. These types of studies are limited by difficulties in the assessment of long term exposures, the presence of a myriad of confounding factors and co-exposures to other known carcinogens in food and water. Disinfection by products and even infections make it difficult the establishment strong associations between air pollution and cancer risk factors.

Prostate Cancer There are only two studies in the literature that found an association between prostate cancer and air pollution (Soll-Johanning and Bach 2004; Parent et al. 2013). Recently, a case–control study conducted in Montreal evaluated environmental risk factors for prostate cancer and found associations between

exposures to traffic related air pollution, assessed by exposures to NO_2, and increased risks of prostate cancer incidence. Limitations of the study include exposure assessment based on home address and time of exposure which was 25 years prior to the interview and thus which could misclassify an individual's exposure (Parent et al. 2013).

Breast Cancer In women, breast cancer has the highest incidence rate. Many risk factors have been pointed out such as genetic factors, lifestyle, reproductive history, smoking and alcohol consumption. Although many factors have been identified most of the cases remain with unknown etiology (Coyle 2004). The first evidence of a possible relationship between breast cancer and air pollution levels came from the observation that the incidence was higher in urban areas compared to rural areas (Bako et al. 1984; Hall et al. 2005; Reynolds et al. 2004). Human studies are limited, however there at least 30 substances present in urban air pollution that are known to be associated with increased mammary tumors in animals such as benzene (diesel exhaust) and polycyclic aromatic hydrocarbons (PAHs). Thus, it is plausible that traffic-related exposures may contribute to the incidence of breast cancer (reviewed by Rudel et al. 2007). In the USA, few studies assessed the relationship between air pollution exposure and breast cancer. Lewis-Michl et al. (1996) conducted a case-control interview study in New York (USA) and suggested a possible increased risk [OR = 1.29; 95 % CI: 0.77–2.15] of breast cancer among postmenopausal women who live near areas with high traffic density. Bonner et al. (2005) found that early-life exposures to relatively high concentrations of air pollution (i.e., >140 $\mu g/m^3$) were associated with an increased risk of developing postmenopausal breast cancer (OR = 2.42; 95 % CI, 0.97–6.09). In Canada, Crouse et al. (2010) found evidence of an association between the incidence of postmenopausal breast cancer and exposure to ambient concentrations of NO_2. In China, Huo et al. (2013) have shown that long-term air pollution exposure may contribute to the development of breast cancer.

Ovary Cancer In the literature, there are only two studies that have found an association between air pollution and ovarian cancer. In the first study published in 2005, Iwai et al. (2005) conducted a cross-sectional epidemiological study using the annual vital statistics and air pollution throughout Japan and found that breast, endometrial, and ovarian cancer showed significant increases in mortality rates in relation to particulate pollution. More recently in Taiwan, Hung et al. (2012) showed that individuals who resided in municipalities with higher $PM_{2.5}$ levels were at a significantly increased risk of death from ovarian cancer.

2.4 Experimental Evidence

All of the published studies acknowledged that there are many uncertainties on the association between adverse reproductive outcomes and air pollution (Pope 2000; Chen et al. 2008; Valavanidis et al. 2008; Ren and Tong 2008). Undoubtedly these

aspects point out that there is a need for further toxicological and clinical studies to confirm, to strengthen and elucidate the mechanism involved in this association, to identify most susceptible subgroups and to create ways to reduce these impacts on human health. The scientific literature is extremely scarce with regard to experimental studies conducted to evaluate reproductive efficiency using laboratory animals exposed to real urban air pollution. Available studies conducted on experimental animals, mainly mice, have corroborated human epidemiological data and have provided data showing additional effects not yet investigated in humans.

Studies using a multigenerational mouse model of exposure to "real world" ambient concentrations of air pollution, (i.e. mice mates and their litters were continuously exposed inside chambers to either filtered-clean air or non-filtered air-polluted air), found that urban air pollution compromises reproductive health in different ways across generations. This series of studies has shown that in the first generation (G1) of mice exposed to air pollution there were significant reductions in the number of viable fetuses, increased numbers of implantation failures, and a decreased male/female secondary sex ratio (Mohallem et al. 2005; Lichtenfels et al. 2007). In the second generation of mice (G2), females exposed to air pollution during gestation gave birth to litters with reduced birth weights, but no differences in litter size and viable fetuses were observed. Birth weight was significantly lower with a mean reduction of 21 % compared to fetuses from non-exposed females (Veras et al. 2009).

The negative effect of air pollution exposure during pregnancy and birth outcomes are increasingly recognized, but most epidemiological studies have focused only on exposure during the gestational period. Evidence from animal studies explored the effects of maternal exposure before pregnancy on fetal development and demonstrates that maternal exposure not only during pregnancy, but also before conception, adversely affected fetal birth weight (Veras et al. 2008; Rocha et al. 2008). In the same way, exposure to air pollutants during gestation and/or during the pre-gestational period was associated with increased post-implantation loss rates in exposed females (Veras et al. 2009). These results support the findings from Perin et al. (2010a, b) on the importance of the pre-gestational period on gestation establishment. Examination of the placenta from dams exposed to air pollution before and/or during pregnancy revealed that both pre-pregnancy and pregnancy periods of exposure to polluted air resulted in morphological changes in the placenta (Veras et al. 2008). Veras et al. (2008) found that decreases in fetal weight were accompanied by decreases in the volume of maternal blood spaces, in the mean diameter of maternal blood spaces, and in maternal:fetal surface ratio. These features were accompanied by increases in the surface area of fetal capillaries, the total diffusive conductance of the intervascular barrier, and the mass-specific conductance of that barrier. None of the studies conducted in human has evaluated whether placental changes are associated with adverse pregnancy outcomes in humans. Recently, van den Hooven et al. (2012a) using ultrasound measurements and markers of placental growth and function have shown that in human the placenta development, as observed in animals, is impaired by maternal exposure to air pollution.

Umbilical cords were also evaluated and exposures to air pollution were associated with thinner and less voluminous umbilical cords (loss of mucoid connective tissue and collagen content). Structural changes in umbilical arteries and veins and elevated immunoreactivity for 15-F2t-IsoP (oxidative stress), ETAR and ETBR (vascular tone) in their walls were found. Together these findings indicate compromised fetal development evidenced by reduced birth weight might be mediated by alteration in placental and umbilical structure and function as well as by imbalances in the endogenous regulators of vascular tone and oxidative stress (Veras et al. 2012).

The reproductive capacity of G2 nulliparous female mice was also examined and results have shown changes to estrous cyclicity and in ovarian follicle counts (decreased numbers of antral follicles) (Veras et al. 2009). Antral follicles represent the last stage in follicle development prior to ovulation and are the only follicle type capable of releasing an oocyte for fertilization and synthesizing estrogen (Hoyer and Sipes 1996; Hirshfield 1997). Increases in the rate of follicle depletion can potentially raise the possibility of premature ovarian failure and early menopause in the case of humans (Rowe 2006). Observed changes in estrous cyclicity are indicative of persistent estrus, which may reflect an impairment of ovulation as well as changes in the levels of circulating ovarian hormones (EPA 1996).

Further, in the second generation it was observed changes in couple-based outcomes. Couples exposed to air pollution presented decreased fertility indices, decreased pregnancy success and delayed onset of reproductive maturity, as evidenced by extended times to mating (Veras et al. 2009). In humans, air pollution exposures seemed to decrease conception rates (Dejmek et al. 1998). However, we still do not know if the effects are associated with impairments on female or male health.

It is important to point out that the mean concentration of $PM_{2.5}$ (24-h average concentration) used in some studies (27.5 μg/m^3, Veras et al. 2008, 2009), is less than the 35 μg/m^3 established by the U.S. National Ambient Air Quality Standards [US-NAAQS] (http://www.epa.gov/air/criteria.html) and, approximately equivalent to the World Health Organization (WHO) air quality guideline (25 μg/m^3; WHO 2005) raising the question of whether these proposed values are safe for reproductive health.

Two recent mechanistic experimental studies (*unpublished*) addressed the associations between air pollution exposure during the initial stages of pregnancy in mice and uterine response to embryo implantation. Scoriza et al. (2009) observed that in early pregnancy (6 and 8 GD) that reductions in the number of uterine natural killer (uNKcells) and mast cells could contribute to the increased rates of post implantation losses observed in mice. uNK cells are a subpopulation of lymphocytes that in normal mice promote decidual angiogenesis, trophoblast and placental cell growth, provide immunomodulation at the maternal-fetal interface for a healthy pregnancy (Bilinski et al. 2008). The role of mast cells in pregnancy is less known. However, during normal early pregnancy, the number of mast cells and their activation change (Gibbons and Chang 1972; Marx et al. 1999). These data suggest that components present in air pollution may indirectly interfere with or impair

embryonic development through changes to the maternal environment including maternal immune responses. In another study, nulliparous mice were exposed to two different doses of fine particulate air pollution ($PM_{2.5}$) for 45 days before pregnancy until gestational day 4 and expression of different uterine receptivity markers were evaluated (*Lif*, leukemia inhibitory factor; and *Muc1*, mucin, pinopods) as well as uterine histopathology. Histopathology revealed a decrease in the volume and thickness of the endometrium as well as changes in the diameter and thickness of the glandular and luminal epithelia. No significant alteration was observed in the expression (qPCR/IHC) of *Muc1* but there was significant suppression of *Lif* during the window of implantation. These findings suggest that air pollutants may affect the fine regulation of proliferation and differentiation of uterine stromal cells during decidualization via reduced LIF expression (Castro et al. 2013).

Evidences from experimental studies linking and chronic exposure to air pollution are in line with the epidemiological findings (Knottnerus et al. 1990; Peters et al. 1997; Pekkanen et al. 2000). However, the mechanisms involved in this association are not clearly known. There are many suggested potential mechanisms which include induction of p450 enzymes, DNA damage, and systemic alterations in hematocrit, blood viscosity, blood coagulation, endothelial dysfunction, oxidative stress, and inflammation (Baskurt et al. 1990; Sørensen et al. 2003; Andrysík et al. 2011). The mechanisms proposed are described in more detail in the next section.

2.5 Biological Mechanisms

The mechanisms, by which, air pollution could cause adverse health effects are characterized by their ability to directly act as pro-oxidants of lipids and proteins or as free radical generators, promoting oxidative stress, inflammatory responses and damage to mitochondrial function (Menzel 1994; Rahman and MacNee 2000; Li et al. 2003).

The first system to in contact with air pollution is the respiratory tract. Epidemiologic and experimental data show that the air pollution can cause pulmonary inflammation, decrease of pulmonary function, and aggravation of pre-existing pulmonary diseases such as asthma and bronchitis (Laumbach 2010; Saldiva et al. 2002; Seaton et al. 1995).

The bigger fraction of the PM gets trapped on the superior respiratory tract, and the smaller fraction can reach the lungs and these particles can be deposited (Amdur and Corn 1963; Amdur and Creasia 1966). In an attempt to remove such particles, alveolar macrophages phagocytize the particles, penetrating into the cellular interstitium, but part of these fine particles can be translocate across the air–blood barrier into circulation and towards secondary target organs, suggesting that the smaller the particle diameter, the greater the possibility of translocation to other organs (Takenaka et al. 1986; Ferin et al. 1992; Oberdorster and Utell 2002; Chen et al. 2006).

The majority of fine and ultrafine (<$PM_{0.1}$) particles found in the urban atmosphere derive from engine combustion. Ultrafine particles have very low mass typically with magnitudes higher particle numbers and therefore a high surface area relative to fine and coarse particles for adsorption of toxic species (Sioutas et al. 2005). Studies suggest that only a small fraction of PM can pass rapidly into systemic circulation, and that pulmonary inflammation seems to play a major role in enhancing the extra-pulmonary translocation of particles (Chen et al. 2006; Brown et al. 2002; Burch 2002; Mills et al. 2006; Wiebert et al. 2006a, b; Möller et al. 2008). Organic components of particles, which comprise a large proportion of freshly emitted exhaust and secondary aerosols, can induce a broad polyclonal expression of cytokines and chemokines in respiratory epithelium and this effect may be due to the action of PAHs, metals and related compounds that lead to the production of cytotoxic reactive oxygen species (ROS); and these inflammatory and oxidant stress responses are expected to occur at extra-pulmonary sites, as well (Sioutas et al. 2005; Ritz and Wilhelm 2008).

Several hypotheses have been proposed that air pollution can affect the reproductive system causing negative effects, such as impairment of male and female reproductive capacity, placental alterations and fetal health.

As we have previously described, exposure to air pollution is associated with detrimental pregnancy outcomes and these outcomes can be caused by a combination of maternal, fetal, and placental factors or a combination of them. . For example, air pollution can affect the utero-placental and umbilical cord flow and consequently the transport for glucose and oxygen though the placenta (Veras et al. 2008, 2012; Ritz and Wilhelm 2008; Vorherr 1982).

According to the review of Kannan and collaborators (Kannan et al. 2006, 2007), the particulate matter present on the air pollution can affect pregnancy outcomes due to:

- Increase in oxidative stress: an important mechanism of action PM can be the DNA damage induced by oxidative stress, also some metals in PM may inhibit the DNA repair enzymes.
- Inflammation: Inflammation could be associated with inadequate placental perfusion and impaired transplacental nutrient exchange, which may cause growth restriction in utero due to interference with some process or processes such as affecting nutrition of the fetus, reduced oxygenation of maternal blood, or both.
- Coagulation and blood pressure: PM exposures may increase any of the proteins of the clotting cascade, indicating a higher possibility for coagulation and may also lead to changes in hemoglobin, platelets, and white blood cells, which may potentially contribute to adverse fetal growth. PM exposure is also associated with elevations on the blood pressure in pregnant women and this could increase the risk of adverse outcomes, especially if there is preexisting hypertension (pregnancy-induced or not). Elevation of blood pressure in pregnant women has been associated with IUGR and preterm delivery.
- Hemodynamic responses: an impaired adaptation of maternal hemodynamic may lead to an impaired fetal growth. These changes may force the fetus to

adapt, down-regulate growth, and prioritize the development of essential tissues.

- Endothelial function: PM exposure may cause endothelial dysfunctions leading to vasoconstriction and could be considered as an intervening pathway in subsequent impact on fetal growth.

These pathways may or may not act independently, but it is more likely that the outcomes of the exposure to air pollution are an association among these pathways and they are probably related to the composition of the particulate matter (Saldiva et al. 2002).

There are evidences that the air pollution can affect not only the pregnancy but also the male and female reproductive fertility (Somers and Cooper 2009).

Based on epidemiological studies it was observed that exposure to air pollution affects fertility rates (Dejmek et al. 2000; Selevan et al. 2000) at different seminal parameters, motility and morphology and the sperm DNA (Rubes et al. 2005; Hansen et al. 2010; Jafarabadi 2007).

In a study conducted by Somers et al. (2002), a significant elevation in mutation frequency was reported in the offspring of animals exposed to air pollution; primarily through expanded simple tandem repeat (ESTR) DNA loci mutation events in the paternal germline.

In other studies conducted by Somers et al. (2004) and Yauk et al. (2008), they noted that ESTR mutation frequencies were also elevated the paternal germline of mice exposed to whole ambient air at the polluted industrial site, indicating that mutations were induced in spermatogonial stem cells. Maternal ESTR mutation frequencies were similar in all groups, and therefore unaffected by air pollution exposure (Somers et al. 2004). Bulky DNA adducts were not significant, suggesting that DNA reactive chemicals do not reach the germ line and cause ESTR mutation. In contrast, DNA strand breaks were elevated after 3 weeks of exposure, possibly resulting from oxidative stress arising from exposure to air pollution and its particulate matter (Yauk et al. 2008).

Sperm DNA in mice exposed to whole ambient air was globally hypermethylated compared to those exposed to filtered air. These methylation changes appeared early in the environmental exposure and were still present after 6 weeks without the air pollution exposure. Persistent changes in the methylation status of genes may have health implications for the next generation through altered gene expression (Somers et al. 2004; Yauk et al. 2008).

Environmental toxicants can alter the female reproduction by direct mechanisms (hormone disruptors) or indirect (immunological toxicants). Direct effects typically occur if an environmental chemical is structurally similar to a molecule capable of interacting with endogenous reproductive organs. Indirect effects can occur if a chemical interferes with the hormonal action. Natural hormones are critical for development, behavior, puberty beginning, sexual function, and gametogenesis. Some environmental chemicals can mimic or block the action of the natural hormone, thus negatively altering reproductive processes (McLachlan and Arnold 1996).

As steroid hormones, some environmental toxicants are lipo-soluble and cross the cell membrane by passive diffusion, thereby allowing access to any animal cell. Once these chemicals cross the cell membrane, which may interact with steroid receptors, access to the nucleus as a dimer hormone-receptor induces the activation or suppression of genes causing a biological response (McLachlan and Arnold 1996).

Several compounds present in air pollution (heavy metals, environmental oestrogens, diesel and PAHs) are able to suppress or interfere with the regulation of the hypothalamic-pituitary-gonadal axis; resulting in changes in growth and development of ovarian follicles and estrous cyclicity (Veras et al. 2009; Mamatsashvili 1970; Borgeest et al. 2004), affecting the whole process of pregnancy, including signaling pathways between the conceptus-mother or, the uterus preparation for implantation (Hoyer and Sipes 1996; Mattison and Thomford 1989; Tsukue et al. 2001; Takeda et al. 2004; Telisman et al. 2007). However, the specific contaminants that caused sperm damage and the potential impact on fertility or pregnancy outcomes were undetermined (Somers 2011).

PAHs in air pollution have the capacity to bind to steroid receptors, mimicking their action, and thus altering the production of these hormones, which can result in adverse consequences for the development and reproductive health (Kristensen et al. 1995; Wenger et al. 2009; Han et al. 2010). For example, Hood (2006) in his study suggests that exposure prior to conception, both female as male, can lead to a hormonal dysregulation causing direct damage to the reproductive organs and gametes.

Studies suggest that PAHs are able to cross the placenta and reach fetal organs causing adverse reproductive outcomes, including; stillbirths, reabsorptions, congenital abnormalities, and decreases in fetal weight. The exposure to PAHs may lead to increased DNA adducts, resulting to LBW and intrauterine growth restriction. Furthermore, the PM may bind receptors for placental growth factors leading to decreased fetal-placental exchange of oxygen and nutrients (Dejmek et al. 2000; Ritz and Wilhelm 2008).

2.6 Prevention

There are sufficient evidence of the harmful effects of exposures to environmental air pollution on reproductive health. Furthermore, it is clear that increased levels of air pollution are found in developing and underdeveloped countries in regions with high population density and higher fertility rates (Fig. 2.1). Although the risks associated with the negative reproductive outcomes tend to be small, the number of people that might be affected is significantly large. Furthermore, if we consider that negative influence on the initial stages of life (embryo/fetus) increases the risks of later life diseases, such as diabetes, metabolic syndromes and cardiovascular diseases (Osmond and Barker 2000; Gluckman and Hanson 2004) exposures to air pollution during pregnancy would have a profound impact in public health strategies to prevent most common health issues

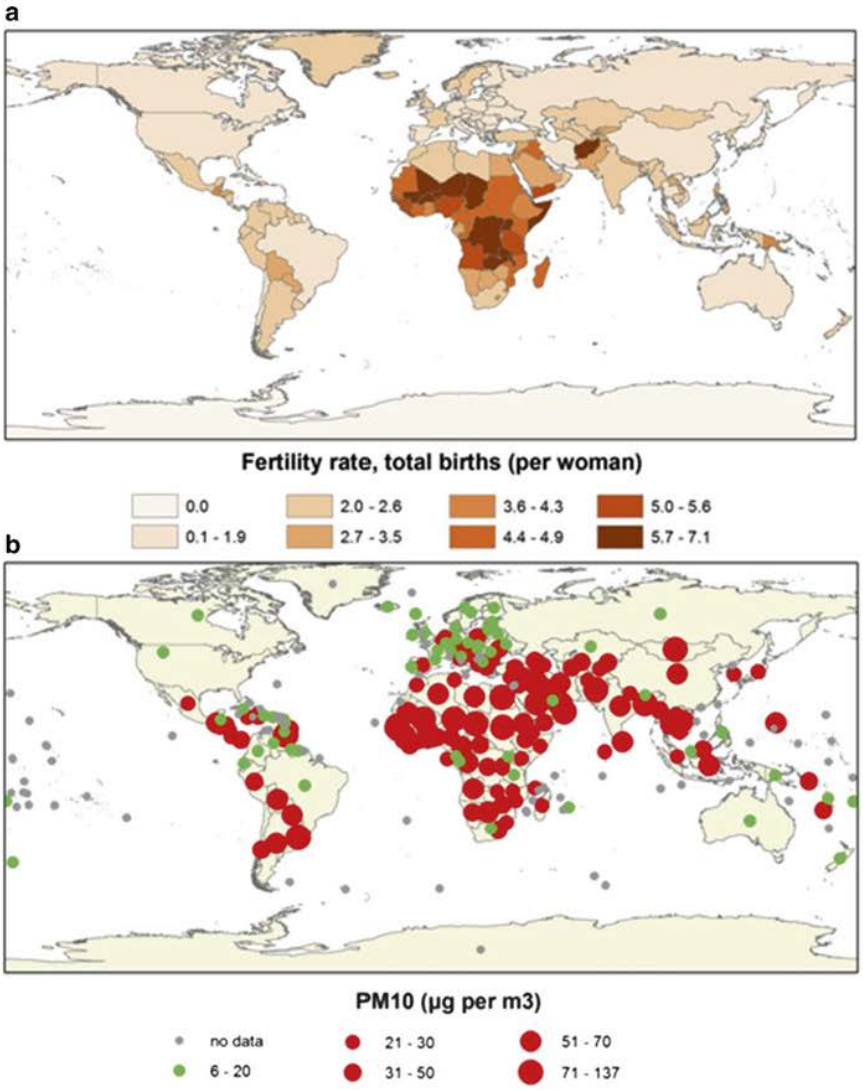

Fig. 2.1 Global scenario of gestational exposure to air pollution. The map compares the total births per women in 2009 (data from the World Bank) (**a**) (World Bank 2013a) with the annual mean concentration of particulate matter of 10 µm or less (PM10) in the same year (data from the World Bank) (**b**) (World Bank 2013b), showing that reproductive health consequences from air pollution exposure is a major concern in the developing nations where a growing population is being exposed to levels of particulate air pollution above the WHO recommended limits

The most effective way to reduce health risks associated with air pollution is to implement air quality management strategies and National Air Quality Standards (Thurston and Balmes 2012). The U.S. Environmental Protection Agency (EPA) projections that by 2020 adherence to the Clean Air Act standard for ozone alone will prevent 230 million premature deaths and 280 infant–mortalities (EPA 2011). Indeed, increasingly stringent (NAQS) already proved effectiveness in improving air quality in the United States and Western Europe in recent decades (Van Erp et al. 2008) and a global analysis concluded that flexible air quality standards lead to higher air pollution concentrations (Vahlsing and Smith 2012).

2.7 Concluding Remarks

Epidemiologic and experimental evidences converge to indicate that air pollution, at the current levels, play a deleterious role on reproductive function. In addition to the scientific questions raised from the aforementioned evidences presented in this chapter – which are the mechanisms, which are the most important pollutants or are the observed effects the result of a mixture of mixtures – some ethical considerations emerged at this moment. Indeed, the options of energy use, industrial production and mobility made by our and our preceding generations, may be affecting those that did not participate in the decision process. Moreover, there is a marked contrast in ambient air pollution concentrations, creating an uneven attributable risk across the globe. As a general rule, air pollution is the result of bad technologies, usually present in the less privileged countries. These points deserve serious consideration when translating knowledge into public policies aimed to protect children globally.

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4.4.2. Capítulo de livro para a Coleção Sofia Belas Artes: Encontro de Saberes

Neste capítulo[25] utilizei evidências científicas da literatura sobre as relações entre a cidade e qualidade de vida para construir uma narrativa para o público instruído em outras áreas do saber. Publicado em 2015, textos de cientistas e especialistas em artes, arquitetura, ciências sociais e ciências humanas também compõe o livro. A seguir apresento na íntegra o capítulo que escrevi juntamente com meu orientador.

7

Como as cidades moldam a saúde de seus moradores?

Paulo Saldiva &
Laís Fajersztajn

Paulo Saldiva

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O modo como a sociedade está organizada e o estilo de vida promovido pelas cidades tem papel fundamental nas mudanças do perfil de saúde nas áreas urbanas, correspondendo atualmente a 84% da população brasileira. Por muitos séculos, as cidades apresentaram piores condições de saúde. A densidade populacional favorecia a emergência de epidemias de cólera, diarreia e outras doenças infecciosas. Com o avanço das descobertas científicas quanto às formas de transmissão de doenças (início do século XIX), as cidades começaram a se estruturar com o objetivo de promover a saúde pública, principalmente a partir da adoção de medidas sanitárias. Os serviços de assistência à saúde acompanharam o desenvolvimento científico-tecnológico, tornando muito mais eficientes os centros urbanos, e assim, viver nas cidades passou a ser uma vantagem para a saúde, comparado com a vida rural.

Atualmente, doenças e agravos não transmissíveis como hipertensão, diabetes e obesidade prevalecem nas cidades, e respondem por quase 80% da mortalidade geral e dos gastos do Sistema Único de Saúde (SUS) com internações no município de São Paulo. Por muito tempo, as autoridades de saúde focaram esforços – com sucesso – na modificação de fatores individuais de risco, tais como o controle medicamentoso do colesterol, glicemia e pressão arterial, bem como a propagação de comportamentos saudáveis (parar de fumar, praticar atividade física, alimentação saudável, dentre outros). No entanto, a promoção da saúde pública poderia ser muito mais efetiva se suas estratégias estivessem sistematicamente integradas a políticas relacionadas à organização e funcionamento geral da cidade.

A lei antifumo mostra como o funcionamento de uma cidade pode melhorar a saúde de sua população: a proibição de fumar em ambientes fechados de uso coletivo diminuiu o tabagismo secundário e a quantidade de cigarros/dia entre os fumantes. Em contrapartida, a imobilidade no município de São Paulo gera um custo anual estimado em mais de R$ 40 bilhões, valor equivalente a 1% do produto interno bruto brasileiro. A saúde é afetada não só por conta do tempo perdido no congestionamento e

por impactos nocivos à saúde, tais como a exposição à poluição do ar, em certa medida estimados no cálculo, mas também pela contribuição desse fator para a obesidade, estresse emocional e outros agravos.

Ademais, o progresso que resultou na vantagem para a saúde de viver nas cidades não atingiu todos os moradores urbanos. Ainda hoje, populações de baixa renda, particularmente aquelas residentes em favelas, convivem com a falta de saneamento básico, tendo dificuldade de acesso aos serviços de saúde. Riscos característicos do passado, como diarreia e infecção por leptospirose, ainda são mais frequentes nessa parcela da população. Soma-se a isso, a influência negativa de determinantes sociais – escolaridade, renda e outros – nos desfechos de saúde desta parcela da população.

Por fim, a violência urbana diminui o desempenho de saúde da população como um todo, seja causando diretamente mortes e incapacidades, seja prejudicando a saúde mental ou restringindo a mobilidade e o lazer dentro da cidade.

Durante as décadas passadas, a Organização Mundial da Saúde tem tentado fortalecer as relações entre saúde e planejamento urbanos através de dois movimentos, ainda pouco robustos na América Latina: Saúde em todas as políticas (*Health in all policies*) e Movimento das cidades saudáveis (*Healthy cities movement*). Em paralelo, a preocupação da comunidade de saúde com os impactos das mudanças climáticas tem crescido, sendo outra abordagem possível para fortalecer a comunicação entre ambiente construído e indicadores de saúde. Em 2009, uma série de artigos publicados no *The Lancet* indicaram que algumas ações que reduzem a emissões de gases de efeito estufa trazem benefícios para a saúde da população local onde tais medidas foram adotadas. Em 2015, a mesma revista alertou: combater as mudanças climáticas pode ser a melhor oportunidade de saúde do século XXI. No artigo, a revista recomendou a transição para cidades que promovam estilos de vida saudáveis para as pessoas e para o planeta, dentre as resposta para mitigar as mudanças climáticas (Watts et al., 2015). Como as populações de baixa renda são mais vulneráveis aos impactos das mudanças climáticas em todas as escalas (entre nações e entre cidades), combater as mudanças climáticas pode também ser uma oportunidade para reduzir as desigualdades de saúde.

O desafio de moldar cidades que promovam a saúde de seus moradores é complexo e requer esforço multidisciplinar para além das competências tradicionais do setor de saúde no Brasil. Nos Estados Unidos, um experi-

mento conduzido pela universidade de Harvard com 4.600 famílias, mostrou que prover auxílio moradia para que famílias de baixa renda se mudem para bairros melhores melhora significativamente a saúde física e mental de crianças e adultos. Além de indicar que os bairros modulam de forma diferente a saúde de seus moradores, o estudo aponta uma possível estratégia de promoção da saúde pública a cargo de outras esferas de governo, que não o setor saúde (Chetty et al., 2015). No mesmo direcionamento, os níveis de poluentes atmosféricos caíram acentuadamente em Dublin após o banimento do uso do carvão na cidade, resultando em redução significativa da mortalidade por causas cardiovasculares e respiratórias em apenas três anos (em 10% e 16% respectivamente)(Clancy et al., 2002).

Habitação e mobilidade são diretrizes fundamentais do planejamento urbano que modulam grande parte das associações conhecidas entre ambiente construído e saúde. Neste artigo discutimos alguns dos impactos da mobilidade e da habitação na saúde da população urbana, além dos impactos de outras estruturas urbanas.

O custo anual da imobilidade na cidade de São Paulo equivale a 7,5% do produto interno Bruto da cidade (Cintra, 2014), com impactos significativos sobre a saúde humana. Os mais estudados são os relacionados à poluição do ar (local e emissão de gases de efeito estufa), tempo de deslocamento, ocorrência de acidentes e realização de atividade física. A imobilidade ainda influencia a saúde mental, por motivos relacionados à segurança pública e à interação social, dentre outros.

Os veículos automotores são os principais responsáveis pelos altos índices de poluição do ar na cidade de São Paulo, que chega a reduzir em cerca de três anos a expectativa de vida média do paulistano. Atualmente, melhorias na qualidade do ar advindas dos avanços tecnológicos na engenharia dos veículos e combustíveis tem sido suplementadas pelo aumento da frota e diminuição na velocidade dos veículos.

A poluição do ar tem efeitos agudos e crônicos reconhecidos. Além do desconforto geral (ardor nos olhos, alergias e etc.), a exposição de curto período a altos níveis de poluentes atmosféricos aumenta a internação hospitalar por doenças cardiovasculares e respiratórias. Entre 1996 e 2000, o aumento foi estimado em cerca de 4% para crianças com asma e para adultos com doença pulmonar obstrutiva crônica (Gouveia et al., 2006). A exposição prolongada à poluição do ar aumenta o risco de câncer pulmão e de morrer por causas cardiovasculares e respiratórias. Baixo nível socioeconô-

mico e faixa etária (idosos, crianças e mesmo fetos) representam maior vulnerabilidade, bem como o ser portador de doença crônica ou estar grávida. A exposição à poluição do ar está associada com hipertensão gestacional, baixo peso ao nascer, e prematuridade. Os sistemas endócrino e neurológico, dentre outros, também são negativamente afetados pela poluição do ar. Quando se considera a prevalência do fator de risco na população, a poluição do ar e o tráfego de veículos lideram os fatores de risco para infarto do miocárdio. Isso porque, independente da magnitude do risco individual, toda população urbana está de certa forma exposta à poluição do ar e congestionamentos de veículos (Nawrott et al., 2011).

O Brasil ainda adota padrões de qualidade do ar estabelecidos nos anos 90, que refletem o conhecimento científico dos anos 80. Na prática, níveis de poluição considerados prejudiciais para a saúde de europeus são considerados seguros pelas autoridades brasileiras. Embora sem data para implementação, o estado de São Paulo se comprometeu a adotar os padrões de qualidade do ar recomendados pela Organização Mundial de Saúde. Políticas de controle da emissão de poluentes veiculares, como as relacionadas no PROCONVE (Programa de Controle da Poluição por Veículos Automotores) tem papel decisivo na melhoria dos níveis de poluição do ar urbano. Por diminuírem o número de carros privados nas ruas, políticas de promoção do transporte público e ativo (andar a pé ou de bicicleta) também melhoram a qualidade do ar.

Os acidentes nas vias da cidade de São Paulo resultaram em 1.249 mortes em 2014, 32,5% eram motociclistas. O impacto na morbidade é ainda maior, embora seja mais difícil de ser estimado, por causa da falta de dados. A qualidade das calçadas também está associada a acidentes e incapacidades, e influencia o nível geral de atividade física da população, em especial de idosos e portadores de mobilidade reduzida.

A mobilidade nas cidades influencia como as pessoas utilizam seu tempo. As horas perdidas nos congestionamentos reduzem o tempo para outras atividades como trabalho, lazer e descanso, implicando em consequências para a economia da cidade e para a saúde da população. Estudos tem mostrado que, quanto mais horas jovens de baixa renda perdem em trânsito, menor o potencial de aumento de sua renda familiar no futuro, reforçando as desigualdades sociais. O número reduzido de horas dedicadas ao estudo explica parte do efeito. Ainda, o aumento do tempo de deslocamento tende a aumentar o número de motoristas que infringem a lei e usam dispositivos móveis durante o percurso, aumentando o risco de acidentes.

O tipo de mobilidade oferecida por uma cidade favorece ou não o sedentarismo, fator de risco para diversas doenças crônicas e, prevalente em mais de 50% da população maior de 15 anos do Brasil. Estudos mostraram que o uso mais frequente de transporte ativo estava relacionado com risco reduzido de sobrepeso e com pressão arterial mais baixa (Laverty et al., 2015). Além disso, a mobilidade influencia a exposição ao ruído, afetando a qualidade da audição, do sono, da interação social, entre outros. A exposição crônica ao ruído do tráfego está relacionada ao ganho de peso (Christensen et al., 2015) e alterações cardiovasculares (Halonen et al., 2015).

Por fim, a mobilidade influencia a interação social e a saúde mental de formas fáceis de serem percebidas, como a cordialidade no trânsito ou o receio de furtos durante longos períodos de imobilidade, mas ainda difíceis de serem mensuradas.

As opções de mobilidade que promovem a saúde humana e ambiental são o transporte público e ativo (andar a pé ou de bicicleta). As características ideais dessas formas de mobilidade incluem: segurança, conforto, acessibilidade (tanto em termos de custo financeiro, quanto no que diz respeito ao acesso das pessoas com mobilidade reduzida) e eficiência (em termos de gasto de energia, emissão reduzida de poluentes, tempo e cobertura de todo o território da cidade). O metrô é um exemplo de transporte público que atende a esses requisitos. Além da eficiência no tempo de deslocamento, o metrô contribui para a redução da poluição do ar e consequentes custos com internações hospitalares. Análise custo-benefício do metrô de São Paulo mostrou que os ganhos ambientais e sociais superam os gastos elevados de construção e operação (da Silva et al., 2012).

Uma revisão sistemática recente mostrou que os benefícios para a saúde do transporte ativo superam eventuais riscos por conta da exposição aumentada a acidentes de trânsito e à poluição do ar (Muller et al., 2015). A melhoria da qualidade das calçadas e faixas exclusivas para bicicletas são exemplos de como estimular o transporte ativo.

Em relação à habitação, grande parte das melhorias nas condições gerais de saúde da população urbana teve início dentro das residências, a partir de medidas de saneamento e higiene.

Embora considerados direitos humanos básicos pela Organização das Nações Unidas, o acesso à água potável e ao saneamento não atingiu todos os residentes de cidades, principalmente os residentes de favelas, hoje mais de 11 milhões no Brasil. Como resultado, essas pessoas ainda

convivem com surtos frequentes de doenças infecciosas e mortalidade infantil aumentada, apesar de já existirem meios técnico-científicos disseminados para a redução desse risco. Outras doenças correlatas incluem doenças por vetores (dengue, por exemplo), doenças tropicais negligenciadas (como a esquistossomose) e doenças relacionas a contaminantes químicos presentes na água.

No Brasil, 94% da população tem acesso à água potável. No entanto, a taxa de tratamento do esgoto do estado de São Paulo ainda é de 53,34%, possivelmente porque investimentos em oferta de água potável são percebidos como prioritários comparados à coleta e tratamento de esgoto, tanto pela população quanto pelos governantes.

Apesar dos avanços, a questão do fornecimento de água para as cidades está longe de ser resolvida. Estima-se que os períodos de falta de água nas cidades se tornem mais frequentes com as mudanças climáticas. Em 2015, o nível dos reservatórios de água de São Paulo caiu drasticamente. O período coincidiu com uma epidemia severa de dengue. As mudanças no fornecimento de água e o aumento do armazenamento inadequado de água da chuva podem ter contribuído para o aumento nos casos de dengue em 2015. O armazenamento inadequado de água também impõe riscos para a reincidência de surtos de doenças infecciosas por veiculação hídrica.

Habitações com condições precárias, combinadas à frequente ausência de sistemas de drenagem de água da chuva, aumentam o risco de doenças de veiculação hídrica advindo com as enchentes, como a leptospirose. Muitas regiões urbanas, como o Jardim Pantanal, na zona leste de São Paulo, são sazonalmente acometidas por enchentes. Dependendo da localidade, há também o risco de deslizamentos que, em última instância, levam à morte. Muitas famílias acabam permanecendo em residências inundadas com o intuito de proteger seus bens materiais, indicando também prejuízo da saúde emocional dos acometidos por enchentes.

A qualidade do ar dentro das casas é modulada pela ventilação, níveis de poluentes do ambiente externo e produção de poluentes dentro do ambiente. A fonte de poluição interna mais estudada é a queima de combustíveis sólidos para cozinhar e aquecer a residência. Os impactos para a saúde incluem aumento no risco de pneumonia em crianças menores de cinco anos e doença pulmonar obstrutiva crônica, doenças cardiovasculares, catarata e câncer de pulmão em adultos. Felizmente, a maioria das habitações urbanas brasileira possui fogão.

A fumaça do tabaco também é uma fonte reconhecida de poluição do ar interna. Políticas de restrição do fumo em ambientes fechados, como já é feito para ambientes de uso coletivo em diversas cidades do Brasil, foram efetivas na redução da exposição. O controle dentro das residências é mais difícil.

Carcinogênico, o amianto foi banido na maioria dos países desenvolvidos. Outros países na América Latina, como Argentina, Chile, Uruguai e Honduras, também baniram a substância. Evitar o uso de materiais com amianto e outros componentes tóxicos, como o formaldeído, é uma recomendação prioritária para melhorar a qualidade do ar dentro das residências.

Melhorias na ventilação e iluminação solar das residências e medidas específicas para garantir o conforto térmico, frente a extremos de temperatura, também melhoram a qualidade do ar interior. Materiais específicos de construção e vegetação tem papel fundamental na manutenção do conforto térmico do ambiente. A saúde respiratória é a grande beneficiada. No entanto, como temperaturas interiores baixas tem sido associadas com maior risco para hipertensão arterial, melhorias do conforto térmico tendem a melhorar também a saúde cardiovascular. Um estudo recente mostrou que a mortalidade por temperaturas extremas varia significativamente de país para país. Além de possível variabilidade da capacidade fisiológica de adaptação a extremos de temperatura das diferentes populações estudadas, o estudo indica que a infraestrutura de alguns países (conforto térmico da habitação, inclusive) é mais preparada para proteger a população frente a extremos de temperatura do que outros. O frio foi responsável pela maioria das mortes prematuras das populações estudadas, 7,29% (2,38% no Brasil), contra 0,42% por calor extremo (0,70% no Brasil) (Gasparini et al., 2015).

Embora o presente artigo tenha abordado a influência da mobilidade e habitação na saúde da população urbana, as áreas se inter-relacionam. O local onde as pessoas moram, por exemplo, influi no modo e tempo de deslocamento. Além disso, outras características urbanas moldam significativamente a saúde nas cidades. A presença de parques é um exemplo. Parques estão associados a um aumento no nível de atividade física, o que impacta positivamente a obesidade e outras doenças crônicas. Um estudo conduzido nos estados Unidos entre 1993 e 1996 mostrou que crianças com acesso facilitado a parques e programas de recreação apresentavam menores índices de obesidade (Wolch, et al., 2014). Também nos Estados Unidos, um estudo mostrou que comunidades de baixa renda tem acesso restrito a parques, e que os parques costumam ser mais

poluídos em áreas de baixa renda. Não é difícil de imaginar que a situação no Brasil seja semelhante. Ademais, parques são um meio de aumentar a cobertura verde da cidade, o que ajuda a drenar as águas da chuva, prevenindo enchentes, bem como ajudam a mitigar o efeito das ilhas urbanas de calor. "Ilhas urbanas de calor" é a terminologia que caracteriza o aumento de temperatura de áreas urbanas comparado à temperatura prévia na mesma região em anos anteriores ou em regiões do entorno durante o mesmo período. Em São Paulo, a diferença de temperatura entre a zona central e periférica da cidade pode atingir 10°C.

As ilhas urbanas de calor favorecem a formação de um poluente em particular, o ozônio troposférico. Formado na presença de luz, a partir de nitrogênio e compostos orgânicos voláteis liberados pela queima de combustíveis fósseis, o ozônio é fortemente relacionado a crises agudas de asma e alterações cardiovasculares. Entre 1990 e 2013, a mortalidade ajustada por ozônio no mundo aumentou em quase 20% (Forouzanfar et al., 2013).

No verão, a diferença de temperatura entre o centro (quente) e a periferia (menos quente) da cidade aumenta eventos de chuva forte nas partes centrais da cidade, favorecendo enchentes e seus malefícios à saúde. As enchentes, em conjunto com o prejuízo no funcionamento dos semáforos, agravam a imobilidade na cidade.

As ilhas urbanas de calor aumentam os períodos prolongados de temperatura muito elevada, eventos conhecidos como ondas de calor. Fortemente associadas com aumento da mortalidade, as ondas de calor favorecem a concentração de poluentes atmosféricos, aumentando a incidência de doenças relacionadas à poluição já descritas neste artigo. Estima-se que a temperatura média no Brasil possa subir entre 2°C e 4°C até 2100 (Marengo et al., 2009), mas, ao contrário de países desenvolvidos como a Austrália, o Brasil não dispõe de políticas consistentes para proteger sua população dos extremos de temperatura.

O aumento da temperatura do ar ainda influencia a distribuição de doenças causadas por vetores como a dengue. A taxa de incidência da dengue na cidade de São Paulo (casos por 100.000 habitantes) em 2010-2011 foi maior em áreas que combinavam cobertura vegetal restrita e altas temperaturas médias de superfície do que em áreas com ampla cobertura vegetal: 72,3 casos contra 3,2 casos. A alta temperatura (>32oC) foi o principal determinante para a concentração dos casos, superando características socioeconômicas como regiões de baixo nível socioeconômico, moradia precária e alta densidade populacional (Araujo et al., 2015).

A associação das ilhas de calor e mudanças climáticas na temperatura dos grandes centros urbanos tende a aumentar a frequência e intensidade de ondas de calor, períodos de seca e de chuva intensa. O aumento de áreas verdes nos centros urbanos pode resfriar a temperatura do local e do entorno, contribuindo para a mitigação das ilhas urbanas de calor. O uso de matérias com maior potencial reflexivo na superfície de construções também pode auxiliar.

A distribuição dos serviços na cidade também influencia a saúde dos moradores. Um estudo mostrou que crianças que moram em bairros com menos lojas de conveniência e supermercados apresentam menor índice de obesidade. (Shier et al., 2012)

Ademais, as desordens psiquiátricas são mais prevalentes em áreas urbanas que rurais e contribuem para cerca de um quarto da sobrecarga total da doença na América Latina e Caribe. Condições prevalentes em muitas cidades com grande desvantagem socioeconômica, baixo nível de atividade física, baixo nível de interação social e altos índices de violência, podem resultar em doença mental.

Promover mudanças urbanísticas efetivas para uma cidade mais saudável requer a interação multidisciplinar entre diversas pastas do governo, sociedade civil e outros atores da sociedade. Apesar da magnitude do desafio, os benefícios parecem fortes o suficiente para consensos efetivos, afinal, uma cidade que promova a saúde de sua população é interesse de todos. Ademais, uma cidade saudável deveria ser interesse particular dos profissionais de saúde, pois representa um grande auxílio terapêutico no enfrentamento de doenças e promoção da qualidade de vida.

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4. 4.3. Artigo na revista do Instituto de Estudos Avançados

À exemplo do manuscrito descrito no item anterior, neste artigo[10], o tema abordado também foi cidades e qualidade de vida. No entanto utilizei evidências científicas da literatura para construir uma narrativa introdutória do assunto para um dossiê sobre metrópoles e saúde publicado em 2016. O dossiê conta com textos de outros autores específicos para habitação, poluição do ar, assistência à saúde e áreas verdes, além de abordagens do ponto de vista das ciências humanas. A revista é uma das mais acessadas da plataforma de busca *Scielo* e é lida por gestores e demais interessados em políticas públicas. A seguir apresento o artigo na íntegra.

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Como as cidades podem favorecer ou dificultar a promoção da saúde de seus moradores?

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Introdução

MAIS DA METADE da população mundial vive em cidades. Na América Latina – o continente mais urbanizado do mundo –, a população urbana chega a 82%; no Brasil, a 84%. Com tantas pessoas morando em cidades, entender a influência do ambiente construído na saúde das pessoas torna-se assunto prioritário.

Por muitos séculos, o estilo de vida das cidades causou piores condições de saúde, como maior risco para cólera, diarreia, tuberculose e outras doenças infecciosas. A densidade populacional favorecia a emergência de epidemias, e viver em cidades representava uma desvantagem para a saúde em comparação à vida no campo. Com o desenvolvimento científico sobre as formas de transmissão de doenças, iniciado no século XIX, as cidades começaram a se estruturar visando à promoção da saúde pública, principalmente a partir da adoção de medidas sanitárias. Os serviços de assistência à saúde acompanharam o desenvolvimento científico-tecnológico de forma muito mais eficiente nos centros urbanos e o viver nas cidades passou a ser uma vantagem para a saúde, quando comparado com a vida rural.

Hoje doenças diretamente relacionadas à forma como a sociedade está organizada e ao estilo de vida urbano, como hipertensão arterial, diabetes tipo 2 e obesidade, predominam nas cidades. Conhecidas como Doenças e Agravos Não Transmissíveis (Dant), essas doenças foram responsáveis por 76% da mortalidade geral, 63% das internações pagas e 73% dos gastos do Sistema Único de Saúde (SUS) com internações no município de São Paulo, segundo dados do site oficial da prefeitura. A estratégia de enfrentamento tem se baseado principalmente na modificação de fatores de risco individuais, com resultados positivos, porém limitados, visto que o ambiente urbano pode facilitar ou dificultar hábitos individuais saudáveis, como a prática de atividade física ou a ingestão de frutas e vegetais. Sendo assim, a integração de políticas de promoção da saúde coletiva

e de urbanismo resultaria em ganhos de saúde significativos para os moradores de cidades.

Alguns exemplos bem-sucedidos de controle e prevenção de doenças a partir da modificação de fatores de risco individuais incluem o controle medicamentoso da pressão arterial e colesterol, parar de fumar, alimentar-se de forma mais saudável e praticar atividade física. A lei antifumo, que proibiu fumar em ambientes fechados de uso coletivo no estado de São Paulo em 2009, diminuiu a exposição dos não fumantes à fumaça do tabaco. Tal lei ainda resultou na diminuição da quantidade de cigarros/dia entre os fumantes, sendo um exemplo concreto de como o funcionamento de uma cidade pode melhorar a saúde de sua população. Com custo anual estimado em mais de R$ 40 bilhões, valor equivalente a 1% do PIB brasileiro (Cintra, 2014), a imobilidade no município de São Paulo é um exemplo oposto. A crise de mobilidade afeta a saúde não só por conta do tempo perdido no congestionamento e impactos nocivos da exposição à poluição do ar à saúde, em certa medida estimados no cálculo, mas também pela sua contribuição para a obesidade, estresse emocional, entre outros. Numa cidade congestionada, crianças não brincam na rua e adultos não retornam para almoçar em casa, costume prevalente em São Paulo quando a obesidade ainda não era uma epidemia.

Ademais, o progresso que resultou na vantagem para a saúde de viver nas cidades não atingiu todos os moradores de países em desenvolvimento. Ainda hoje, populações urbanas de baixa renda, particularmente residentes de favelas, ainda convivem com a falta de saneamento básico e condições seguras de moradia. Frequentemente essas populações sofrem com enchentes, falta de água, surtos de doenças infecciosas, entre outros riscos para a saúde, cujas formas preventivas são amplamente evitáveis e conhecidas. Além disso, determinantes sociais como escolaridade, moradia, alimentação e renda exercem influência negativa em moradores de favela, prejudicando ainda mais o desempenho em saúde dessa parcela da população. Por fim, a violência urbana diminui o desempenho da saúde de toda a população, seja causando mortes e incapacidades diretamente, seja prejudicando a saúde mental, ou ainda, restringindo a mobilidade e lazer dentro das cidades. A Região Metropolitana de São Paulo (RMSP) lidera a prevalência de desordens mentais no mundo, quase 30% da população apresentam algum distúrbio como ansiedade e abuso de substâncias, segundo estudo realizado por Andrade et al. (2012). Os pesquisadores mostraram que a exposição à violência (como ter presenciado um assassinato ou ter sido roubado) estava significativamente associada com as desordens mentais e, quanto maior a exposição à violência, a gravidade da doença também tendia a ser maior (Andrade et al., 2012).

Durante as últimas décadas, a Organização Mundial da Saúde (OMS) tem tentado fortalecer as relações entre saúde e planejamento urbano por meio de dois movimentos: Saúde em todas as políticas (Health in all polices) (Ollila,

2011) e Movimento das cidades saudáveis (Healthy cities movement) (Rydin et al., 2012); no entanto, esses movimentos ainda não são fortes nas cidades latino-americanas.

Recentemente, a preocupação da comunidade de saúde com os impactos das mudanças climáticas tem crescido, sendo outra abordagem possível para fortalecer a comunicação entre ambiente construído e melhor desempenho de indicadores de saúde. Em 2009, uma série de artigos publicados no *The Lancet* indicou que algumas ações que reduzem as emissões de gases de efeito estufa trazem também benefícios para a saúde da população onde as medidas foram adotadas (Haines et al., 2009). Em 2015, a mesma revista alertou para o fato de que combater as mudanças climáticas pode ser a melhor oportunidade de saúde do século XXI (Dora et al., 2015; Watts et al., 2015). Como as populações de baixa renda são mais vulneráveis aos impactos das mudanças climáticas em todas as escalas (entre nações e entre cidades), combater as mudanças climáticas pode ser uma oportunidade para reduzir as desigualdades de saúde.

O desafio de moldar cidades que promovam a saúde de seus moradores é complexo e requer esforço multidisciplinar para muito além das competências atuais atribuídas ao setor de saúde no Brasil. O experimento "Moving to Oportunity" conduzido pela universidade de Harvard com 4.600 famílias mostrou que prover assistência para que famílias de baixa renda se mudem para bairros mais saudáveis melhorou significativamente a saúde física e mental de crianças e adultos (Chetty et al., 2015).

Neste artigo propomos uma discussão das relações entre o ambiente construído e a saúde coletiva a partir dos cinco tópicos propostos por Rydin et al. (2012): a) transporte, mobilidade e atividade física; b) produção urbana de alimento; c) ilhas urbanas de calor; d) conforto térmico e qualidade do ar de ambientes fechados (*indoor*); e e) saneamento.

a) Transporte, mobilidade e atividade física

O custo anual da imobilidade na cidade de São Paulo equivale a 7,5% do PIB da cidade (Cintra, 2014), com impactos significativos para a saúde dos moradores. Os veículos automotores são os principais responsáveis pelos altos índices de poluição do ar aos quais os paulistanos estão expostos. Estima-se que a poluição do ar em São Paulo reduza em cerca de 3,5 anos a expectativa de vida média desta população.

O meio de transporte utilizado por um indivíduo em seu dia a dia pode ser determinante para sua saúde. De fato, transporte é um dos determinantes sociais da saúde, segundo a Organização Mundial da Saúde (OMS). Além disso, as emissões veiculares que contribuem tanto para a poluição do ar urbano quanto para as alterações no clima global também impactam diretamente de forma negativa a saúde das pessoas (WHO, 2011).

Por isso, tanto o planejamento quanto as políticas públicas de transporte devem considerar a saúde como um dos critérios de avaliação durante a formu-

lação e mesmo após sua implementação. Na América Latina a inclusão da saúde como um determinante durante esse processo não parece ser uma rotina.

A urbanização latino-americana é caracterizada pela industrialização, pela deterioração ambiental, cidades superpopulosas cercadas por uma periferia pobre, congestionamentos e poucas opções eficientes de transporte público. E o transporte individual em veículos automotores é o modo de transporte prevalente. Contribui para essa escolha o fato de "ter um carro" ser sinônimo de mobilidade, conforto e *status* social (Newman; Kenworthy, 1999).

Olhando sob a perspectiva da saúde, os carros são prejudiciais, pois diminuem a atividade física, contribuem para o isolamento social, causam estresse e a perda de horas de descanso, lazer e trabalho, devido aos congestionamentos. Além disso, colaboram significativamente para a poluição do ar e sonora, e acidentes por automóveis provocam a morte de milhares de pessoas todos os anos (apud McMichael, 1996; Rissel, 2009). A poluição do ar tem efeitos agudos e crônicos reconhecidos. Além do desconforto geral (ardor nos olhos, alergias etc.), a exposição de curto período a altos níveis de poluentes atmosféricos aumenta a internação hospitalar por doenças cardiovasculares e respiratórias (Braga et al., 2002, Saldiva et al., 1992). Entre 1996 e 2000, o aumento de 10 $\mu g/m^3$ do poluente MP10 (material particulado menor que 10 micrometros) associou-se com um aumento nas admissões hospitalares de 4,6% por asma em crianças e 4,3% por doença pulmonar obstrutiva crônica (Gouveia et al., 2006). A exposição prolongada à poluição do ar aumenta o risco de câncer pulmão (Loomis et al., 2013) e de morte por causas cardiovasculares e respiratórias. Baixo nível socioeconômico e faixa etária (fetos, crianças e idosos) apresentam maior vulnerabilidade, assim como ser portador de doenças crônicas ou estar grávida. A exposição à poluição do ar está associada com hipertensão gestacional, baixo peso ao nascer e prematuridade (Stieb et al., 2012). O sistema endócrino (diabetes e obesidade) e o neurocognitivo, entre outros, também são negativamente afetados pela poluição do ar.

A saúde pode ser impactada diretamente de forma positiva pela escolha do meio de transporte que utilizarmos, prevenindo doenças ligadas ao sedentarismo e, indiretamente, pela diminuição dos efeitos causados ao meio ambiente devido às emissões dos escapamentos. As alternativas de transporte benéficas à saúde incluem caminhar, andar de bicicleta e utilizar o transporte público. Entretanto, para que as pessoas utilizem meios mais ativos de transporte, seria necessário que esses oferecessem conforto, segurança, acessibilidade, baixo custo e, principalmente, que fossem integrados de forma a estimular seu uso.

Um dos maiores desafios dos planejadores urbanos é melhorar o transporte urbano em termos de eficiência no deslocamento e diminuição das emissões veiculares. Uma forma de estimular o uso do transporte ativo é integrar ciclovias ao sistema de transporte público. Isso já é empregado na Europa e em alguns

países na América Latina, com excelentes resultados na saúde da população e para o meio ambiente (Pucher; Buehler, 2008; 2007; Gomez et al., 2015).

Um revisão sistemática recente sobre benefício do transporte ativo para a saúde mostra claramente que essa opção gera grandes ganhos apesar dos riscos de acidentes e da exposição à poluição do ar. Os benefícios estão ligados ao fato de o transporte ativo proporcionar um aumento na atividade física e interação social, reduzindo os riscos para doenças como diabetes, hipertensão e obesidade (Muller et al., 2015). E essa é uma questão muito importante de saúde pública, pois 30% dos adultos fazem menos exercício que o recomendado, o que juntamente com uma dieta rica em calorias e gorduras é a principal causa da obesidade.

Na América Latina, ao contrário do que ocorre na Europa e na América do Norte, o apelo para mudanças nas políticas de transporte está relacionado à resolução de problemas de mobilidade (congestionamentos) e os argumentos são praticamente baseados somente em questões econômicas e materiais (Becerra et al., 2013). Os setores da saúde e do do meio ambiente deveriam participar do processo de tomada de decisão sobre mobilidade e os planejadores urbanos deveriam estar conscientes dos impactos que o ambiente construído e dos meios de transporte trazem à saúde física e mental. As iniciativas de estímulo e implementação de alternativas de transporte ativo ou sua integração ao sistema tradicional na América Latina são poucas. Mas em algumas grandes cidades, como Rio de Janeiro, São Paulo, Curitiba, Bogotá, Buenos Aires e Santiago, já se observam mudanças e a implementação de ciclovias integradas como opção alternativas ao transporte individual. Também há em grandes capitais a implantação dos BRT, que são ônibus de trânsito rápido em vias exclusivas (México, São Paulo, Belo Horizonte, Equador). Essas medidas reduzem o número de veículos na rua e, portanto, os níveis de poluentes tendem a cair, e dessa forma também contribuem para uma melhora na saúde geral da população.

O estudo de Laverty et al. (2015) examinou a correlação entre dados sociais e demográficos e o uso de meios de transporte ativo e desfechos específicos de saúde (diabetes, pressão arterial, sobrepeso) de adultos em seis países (México, Índia, China, Rússia, Gana e África do Sul). Os seus resultados mostraram que os indivíduos que realizam seus deslocamentos de forma mais ativa apresentam riscos reduzidos para ganho de sobrepeso e alterações prejudiciais na pressão arterial.

A poluição do ar é o principal fator de risco ambiental para a saúde e o único meio de evitá-lo é reduzindo seus níveis, ou seja, reduzir as emissões. A OMS estima que 1,3 milhão de mortes por ano estejam associadas a exposição à poluição do ar no mundo. Os impactos sobre a saúde incluem uma grande variedade de efeitos que são influenciados por idade, sexo e presença de doenças preexistentes no indivíduo exposto: doenças cardiorrespiratórias, doenças neurodegenerativas, diminuição da fertilidade e câncer (HEI, 2010; Calderón-

-Garcidueñas et al., 2008). A frota de veículos também contribui para a emissão de gases do efeito estufa colaborando de forma efetiva para acelerar as mudanças climáticas e seus impactos sobre a saúde. Temperaturas extremas estão associadas a um aumento de risco para mortalidade por diferentes causas (Anderson; Bell, 2009; Analitis et al., 2008). Um estudo recente de nosso grupo de pesquisa mostrou que variações moderadas na temperatura também estão associadas a riscos aumentados para mortalidade reforçando a importância das alterações climáticas (variações térmicas) na saúde (Gasparrini et al., 2015).

O transporte ativo integrado a um sistema de transporte público eficiente é uma das alternativas para melhorar a saúde humana, reduzir a poluição ambiental e mitigar as mudanças climáticas. O desafio que os planejadores urbanos e formuladores de políticas enfrentam hoje no desenvolvimento de municípios é como implementar isso em um ambiente urbano concebido para favorecer o modo de transporte privado. Em suma, o transporte ativo não é apenas um meio de reduzir a poluição do ar e as mudanças climáticas em médio e longo prazos, mas também uma forma de melhorar a saúde de milhões de pessoas em curto prazo.

b) Produção urbana de alimento

A produção de alimentos em ambientes urbanos não é uma novidade (FAO, 2014). Insegurança alimentar devido à pobreza (Zezza; Tasciotti, 2010; Wolch et al., 2014), guerra (Milbourn; Vail, 2010, Rydin et al., 2012) e desastres naturais (Hara et al., 2013) garantiu a produção urbana de alimentos nas últimas décadas, mesmo que em pequena escala. Com apelos fundados na sustentabilidade ambiental, atualmente a UPA (sigla em inglês para agricultura urbana e periurbana) tem ressurgido nas cidades mais sustentáveis dos países desenvolvidos (Midle et al., 2014; Hara et al., 2013; Rydin et al., 2012). Ao invés de substituir as atuais e eficientes formas de produção de alimentos para suprimento das cidades, a proposta da UPA é conviver com as opções tradicionais. Segundo relatório da Organização das Nações Unidas para a Alimentação e Agricultura (FAO) de 2014, a UPA está presente em muitas cidades da América Latina, principalmente em quintais residenciais e escolas, mas também de forma comercial. Rosario, uma cidade de 1,35 milhão de habitantes na Argentina, tem 800 hortas comunitárias que produzem verduras para 40 mil pessoas. Cerca de 23 mil hectares de terra são dedicados à plantação na cidade do México, e em Cuba, 40 mil pessoas trabalham em hortas urbanas. Os benefícios da agricultura urbana incluem melhorias ambientais, econômicas, sociais e de saúde.

Comparado com outros residentes urbanos, famílias de agricultores consomem mais frutas e vegetais. A baixa ingestão de frutas e vegetais é um dos dez fatores de risco que mais contribuem para a sobrecarga da doença (Lim et al., 2012). Alimentação de qualidade melhora a saúde cardiovascular (Hu et al., 2011) e ajuda a combater outras doenças crônicas não transmissíveis como obesidade (Gatto et al., 2015) e diabetes (Tohill et al., 2004). A UPA cria oportu-

nidades para a prática de atividade física e interação social reforçando os ganhos em saúde já descritos (Rydin et al., 2012).

Os serviços ecológicos da agricultura urbana podem incluir a regulação do microclima local, manutenção da fertilidade do solo e regulação da polinização dependendo da forma como é conduzida, entre outros (Swinton et al., 2007). Quando o alimento é produzido localmente, a demanda por transporte é reduzida, resultando em economia de energia e diminuição na emissão de poluentes atmosféricos. Outros ganhos em potencial incluem a redução de exportação de resíduos sólidos, desde que projetos de compostagem para uso na UPA sejam implementados, e melhor manejo da água de chuva. Isso porque a maior prevalência da UPA aumenta a superfície de cobertura verde permeável na cidade, permitindo a recuperação das reservas de água (Angnotti, 2015) e auxiliando a prevenção de inundações durante períodos chuvosos. Vale ressaltar ainda que o aumento da cobertura verde urbana tem sido relacionado a diversos benefícios à saúde mental.

A UPA também tem potenciais ganhos econômicos diretos. Famílias envolvidas com a UPA diminuem seus gastos com comida e geram renda extra com vendas, caso esta não seja a atividade principal da família (FAO, 2014). Revitalização de comunidades de baixa renda (Angnotti, 2015) e aumento no valor dos imóveis da região da UPA pela melhoria estética da região (Rydin et al., 2012) podem emergir como ganhos sociais e econômicos indiretos.

Os desafios técnicos com a qualidade das sementes, solo, entre outros, são frequentes, mas podem ser superados. O Programa Escola Estufa Lucy Montoro de 2009, que, entre outros, visa estimular a produção de hortaliças e mudas de árvores é um exemplo de apoio da prefeitura de São Paulo para a atividade. Abordagens mais ecológicas de produção podem contribuir para a preservação do meio ambiente como a poluição das águas e para a redução de doenças ocupacionais por exposição a agrotóxicos.

O maior desafio da UPA é o espaço. Entretanto, estratégias urbanísticas, como telhados verdes (Torrenggiani et al., 2012), podem viabilizar a UPA mesmo em cidades altamente populosas.

Por fim, é importante atentar para a alta prevalência de solos contaminados em áreas urbanas. O estudo dos impactos para a saúde de alimentos produzidos em solos contaminados é escasso. Antes de escolher uma área para UPA, é recomendada uma avaliação das condições locais (solo, incidência de luz, oferta de água etc.). A história de ocupação do solo local pode indicar de forma indireta o potencial de contaminação do solo, na ausência de testes de contaminação (padrão de referência). No caso de atividades industriais, postos de gasolina e lavanderias é prudente considerar o solo contaminado. A remediação é frequentemente possível, mas a falta e alto custo de serviços especializados podem ser um impeditivo. Uma alternativa possível é importar solo saudável e plantar em vasos (Rydin et al., 2012; Angnotti, 2015; Kessler, 2013). Para prevenir exposi-

ções nocivas é prudente seguir recomendações de cultivo como as propostas por Kessler (2013) para agricultores urbanos. As recomendações incluem práticas de agricultura (exemplo: cobrir o solo e as passagens existentes com adubo), bons hábitos (exemplo: usar luvas) e critérios de escolha do local da atividade (exemplo: estabelecer a atividade longe de ruas e avenidas).

Ante os potenciais benefícios para a saúde ambiental e humana discutidos, a OMS recomendou que políticas alimentares sejam incorporadas no planejamento urbano (Rydin et al., 2012).

c) Ilhas urbanas de calor

Ilha urbana de calor é a terminologia que caracteriza o aumento de temperatura de áreas urbanas, comparado à temperatura prévia na mesma região em anos anteriores, ou em regiões do entorno durante o mesmo período. Consequência do processo de urbanização, a substituição da cobertura vegetal do solo por prédios, ruas, avenidas e outras construções de infraestrutura absorve a luz solar, irradia calor e retém menos água, comparado a solos com cobertura natural, reduzindo a umidade para evaporação e resfriamento (Berdahl; Bretz, 1997; Sobral, 2005). A redução da cobertura verde, o uso intensivo de combustíveis fósseis e a construção de prédios altos, que atuam como barreiras para a ventilação, podem explicar as ilhas urbanas de calor (Sobral, 2005). No Brasil, um estudo mostrou que a diferença média de temperatura entre o centro e a periferia de uma cidade média (cerca de 1,5 milhão de habitantes) foi de 6 °C (Santos et al., 2013). Já um estudo conduzido na Região Metropolitana do Rio de Janeiro encontrou variabilidades térmicas de até 25 °C entre áreas com diferentes níveis de urbanização (Sena et al., 2014). As ilhas urbanas de calor podem agravar os períodos prolongados de temperatura muito elevada, eventos conhecidos como ondas de calor.

O aumento da temperatura do ar impacta a flora e a fauna, influenciando a disseminação de doenças causadas por vetores como dengue, zika e febre chicungunya (Coelho-Zanotti; Massad, 2012, Laschewski; Jendritzky, 2002). A taxa de incidência de dengue na cidade de São Paulo (casos por 100 mil habitantes) em 2010-2011 foi maior em áreas que combinavam cobertura vegetal restrita e altas temperaturas médias de superfície (29 ± 2 °C) do que em áreas com ampla cobertura vegetal: 72,3 casos contra 3,2 casos. A alta temperatura (>32 °C) foi o principal determinante para a concentração dos casos, superando características socioeconômicas como regiões de baixo nível socioeconômico, moradia precária e alta densidade populacional (Araujo et al., 2015).

Eventos de ondas de calor têm sido associados a aumento da mortalidade. Na Inglaterra e no País de Gales o calor associou-se a aumento da mortalidade de idosos por quase todas as causas no verão no período de 1993 a 2006 (Gasparrini et al., 2012). Um estudo recente, considerando 384 localidades em 13 países, mostrou que temperaturas ambientes desconfortáveis (frio ou calor extremos) foram responsáveis por um aumento de 7,71% (95% CI 7,43–7,91) na

mortalidade. O frio foi o responsável pela maioria das mortes prematuras 7,29% (7,02–7,49), contra 0,42% (0,39 – 0,44) por calor extremo. A grande variabilidade entre os países encontrada no estudo indica uma possível variabilidade da capacidade fisiológica de adaptação a extremos de temperatura das diferentes populações estudadas, mas também, variabilidade na capacidade de adaptação da infraestrutura do país para proteger sua população frente a extremos de temperatura. No Brasil, o frio foi responsável por um aumento de 2,83% (2,34–3,30) das mortes e o calo,r por 0,70% (0,45–0,93) (Gasparrini et al., 2015).

Estima-se que a temperatura média no Brasil possa subir entre 2 °C e 4 °C até 2100, comparado com as médias de temperatura entre 1961 e 1990 (Marengo et al., 2009). No entanto, ao contrário de muitos países desenvolvidos como a Austrália, o Brasil não dispõe atualmente de políticas consistentes para proteger suas populações dos extremos de temperatura.

Modificações no perfil de calor urbano impactam a dispersão de poluentes, a formação de relâmpagos, além de outros processos físicos e químicos do ambiente urbano (Khan; Simpson, 2001). As ondas de calor aumentam a concentração de poluentes atmosféricos nas ilhas de calor urbanas, aumentando a incidência de doenças relacionadas à poluição e já descritas no item "a" deste artigo.

As ilhas urbanas de calor favorecem a formação de um poluente particular, o ozônio troposférico. Formado a partir de nitrogênio e compostos orgânicos voláteis liberados pela queima de combustíveis fósseis, na presença de luz, o ozônio é mais frequente no final da primavera e começo do outono (Hsieh et al., 1999; Andrade et al., 2004). O ozônio troposférico é fortemente relacionado a crises agudas de asma (Andrade et al., 2004), alterações cardiovasculares e inflamação sistêmica, além de aumento da mortalidade (Bell et al., 2014). Entre 1990 e 2013, a mortalidade ajustada por ozônio no mundo aumentou em 19,8% e a morbidade medida em DALY, em 32,5% (Forouzanfar et al., 2015). Idosos são o grupo populacional mais vulnerável (Bell et al., 2014).

Em São Paulo, o gradiente térmico entre a zona central e a periférica da cidade pode atingir 10 °C. Embora São Paulo tenha duas estações bem definidas: primavera-verão (quente e úmido) e outono-inverno (frio e seco), eventos extremos de temperatura têm se tornado mais frequentes na cidade, particularmente pela influência das mudanças climáticas (Bornstein; Lin, 2000). No inverno, a qualidade do ar fica frequentemente prejudicada em São Paulo e a população tem que enfrentar os efeitos deletérios da poluição para a saúde humana descritas no item "a" deste artigo. Como a disponibilidade de energia solar é baixa, a dispersão de poluentes depende em grande parte da força da circulação da ilha de calor (Bornstein; Lin, 2000).

No verão, a diferença de temperatura entre o centro (quente) e a periferia (menos quente) da cidade aumenta eventos de chuva forte nas partes centrais da cidade (Freitas et al., 2007), favorecendo enchentes e seus malefícios à saúde como o aumento da incidência de leptospirose. As enchentes também se rela-

cionam ao estresse emocional devido aos problemas de imobilidade gerados na cidade e à insegurança da integridade dos bens matérias de pessoas que residem em moradias precárias.

A associação das ilhas de calor e das mudanças climáticas na temperatura dos grandes centros urbanos tende a aumentar a frequência e a intensidade de ondas de calor, períodos de seca e de chuva intensa, com impactos negativos para a saúde e bem-estar de quem vive em cidades. Em Shangai, China, um estudo mostrou que as ilhas urbanas de calor foram diretamente responsáveis por excesso de mortalidade devido a condições extremas de temperatura (Tan et al., 2010). Populações de baixo nível socioeconômico são as mais impactadas (Urban et al., 2014; Burkart et al., 2011).

O aumento de áreas verdes nos centros urbanos pode resfriar a temperatura do local e do entorno, mitigando as ilhas urbanas de calor e seus malefícios para a saúde. Além disso, muitos estudos têm associado o aumento da cobertura urbana verde a ganhos para a saúde mental (Roe et al., 2010) e cardiovascular (Villeneuve et al., 2012). Outros benefícios relatados incluem resultados positivos sobre mortalidade (Villeneuve et al., 2012), desfechos de nascimento (Ebisu et al., 2016), recuperação de cirurgia (Ulrich, 1984), dor de cabeça (Hartig et al., 2003) e sono (Astell-Burt et al., 2013). A literatura também descreve benefícios para a saúde social como redução da criminalidade (Wolfe; Mennis 2012) e melhoria nas interações sociais (Mass et al., 2009).

Qual seria o mecanismo por trás dos benefícios para a saúde da exposição a áreas verdes? A explicação mais consistente até o momento é que a proximidade a áreas verdes incentivaria a prática de atividade física. Assim, os benefícios para a saúde viriam da adoção de um estilo de vida menos sedentário, reduzindo o risco de doenças cardiovasculares, obesidade, entre outros benefícios. Num estudo realizado em cidades de oito países europeus, a frequência da prática de atividade física entre os residentes de áreas mais verdes foi três vezes maior do que a frequência de moradores de áreas menos verdes (Ellaway et al., 2005). Nos Estados Unidos, um estudo mostrou que morar a menos de 500 metros de um parque na infância reduz o risco de sobrepeso na adolescência (Wolch et al., 2011). No Brasil, estudos transversais mostraram que regiões com alta densidade de parques e locais públicos para a prática esportiva estão associados a menor prevalência de sobrepeso em São Paulo (Jaime et al., 2011) e obesidade em Belo Horizonte (Matozinhos et al., 2015).

Outros possíveis mecanismos relacionados aos benefícios das áreas verdes para a saúde são a redução da poluição do ar (Janhall, 2015) e da água (Dora et al., 2015), além de redução da poluição sonora (Fan et al., 2010) e vulnerabilidade de habitações ante enchentes (Dora et al., 2015).

Além do aumento das áreas verdes dentro das cidades, o uso de matérias com maior potencial reflexivo na superfície de construções melhora a eficiência energética do prédio e pode auxiliar na mitigação das ilhas urbanos de calor (So-

lecki et al., 2005). A promoção da agricultura urbana, já discutida no item "b" deste artigo, é uma outra estratégia possível.

d) Conforto térmico e qualidade do ar de ambientes fechados (*indoor*)

A poluição do ar em ambientes internos figura entre os principais fatores de risco para doenças crônicas na América Latina (Lim et al., 2012), e foi responsável por 7% das mortes prematuras na região em 2010 (WHO, 2014). A qualidade do ar em ambientes fechados é modulada por ventilação, níveis de poluentes do ambiente externo e produção de poluentes dentro do ambiente (Rydin et al., 2012). Arquitetos e designers estão na posição de melhorar a ventilação e consequentemente a qualidade do ar interno. A fonte de poluição interna mais estudada é a queima de combustíveis sólidos para cozinhar e aquecer o ambiente interno.

Os impactos para a saúde da poluição em ambientes internos incluem aumento no risco de pneumonia em crianças menores de cinco anos e doença pulmonar obstrutiva crônica, doenças cardiovasculares, catarata e câncer de pulmão em adultos (Smith et al., 2013). Como passam a maior parte do tempo na cozinha ou perto dela, mulheres e crianças pequenas são os mais vulneráveis. A falta de acesso a fontes de energia mais limpas também pode resultar em outros riscos para a saúde como queimaduras, acidentes e intoxicação (Dora et al., 2015).

No Brasil, Fortaleza é a região metropolitana com maior porcentagem de residências sem fogão: 1,76% (IBGE 2010). No entanto, a porcentagem pode ser significativamente maior nos países menos desenvolvidos da América Latina (Smith et al., 2013; Laborde et al., 2015). Fogões movidos a biomassa mais eficientes e com chaminés (idealmente aqueles que resultam em combustão completa) têm sido uma solução bem-sucedida, como mostrado na queda pela metade da incidência de pneumonia em crianças da Guatemala após a instalação desses fogões (Smith et al. 2011). Esses fogões também reduzem as emissões de gases de efeito estufa, beneficiando a saúde pública e mitigando as mudanças climáticas simultaneamente (Wilkinson et al., 2009). O uso de gás ou eletricidade para cozinhar gera pouca ou nenhuma poluição na cozinha. Assim, eletricidade a preço acessível também resultaria em melhor qualidade do ar interior (Smith et al., 2013).

Outras estratégias para adequar a qualidade do ar interno são aperfeiçoamento na ventilação e iluminação solar das residências, aquecimento interno eficiente e uso de materiais de construção que reduzem a perda de calor pelas paredes, janelas e telhados, entre outras estratégias de redução do uso de energia (Rydin et al., 2012).

Intervenções residenciais que promovam o aquecimento e a eficiência energética do lar podem melhorar a saúde geral dos moradores, particularmente pessoas com doenças respiratórias prévias (Thomson et al., 2013). Ademais, temperaturas interiores baixas representam maior risco para hipertensão arterial.

Assim, estratégias de conforto térmico tendem a melhorar a saúde cardiovascular (Shiue; Shiue, 2014).

A fumaça do tabaco em ambientes fechados também é uma fonte reconhecida de poluição do ar interna (Laumbach; Kipen, 2014). Essa exposição pode ser eficientemente reduzida mediante políticas de restrição do fumo em ambientes fechados (Sebrié et al., 2008), como já é feito em diversas cidades no mundo e no Brasil.

O amianto é uma substância carcinogênica (IARC, 2009) relacionada a diversas doenças do pulmão (O'Reilly et al., 2007), incluindo, além de câncer, abestose (Bledsoe et al., 2014). Resistente ao fogo e com propriedades isolantes e de absorção do som, o amianto era misturado ao cimento na construção de materiais, especialmente telhados (Haynes, 2010). O amianto foi banido na maioria dos países desenvolvidos (Laborde et al., 2015). Na América Latina, Argentina, Chile, Uruguai e Honduras também baniram a substância (ibidem). Para melhorar a qualidade do ar interior, seria interessante que arquitetos, engenheiros e demais responsáveis por construções onde o amianto ainda não foi banido optassem por materiais sem amianto na sua composição. O mesmo vale para outros componente tóxicos como o formaldeído (Wang; Zang, 2009).

e) Saneamento

A Organização das Nações Unidas (ONU) considera o acesso à água segura e ao saneamento direitos humanos básicos (United Nations, 2010). A falta de acesso à água segura para beber, saneamento e/ou higiene afeta gravemente a saúde humana (WHO; Unicef 2014). O principal impacto são surtos de diarreia e consequente aumento da mortalidade infantil. No entanto há uma série de outras doenças reconhecidamente relacionadas como desnutrição, doenças causadas por vetores (exemplo dengue), doenças tropicais negligenciadas (exemplo esquistossomose) e doenças relacionadas a contaminantes químicos presentes na água (Freeman et al., 2013; Bartram et al., 2005). Devido à maior prevalência de falta de acesso a fontes de água potável e ao saneamento em populações de baixa renda, estas são as mais vulneráveis (Dora et al., 2015).

Na América Latina, o acesso a água potável para beber atingiu 94% da população em 2012 (WHO; Unicef, 2014). No entanto, mudanças no regime de chuvas, rápido crescimento populacional, alto consumo, falta de planejamento e investimentos, entre outros fatores, desafiam o fornecimento de água potável nos grandes centros urbanos.

A fundação de uma companhia para o fornecimento de água para as residências de São Paulo no final do século XIX foi um marco do início das medidas sanitárias no Brasil. No entanto, o esgoto não recebeu a mesma atenção. A primeira lei para regular a poluição das águas em São Paulo data de 1940. E ainda hoje, a taxa de tratamento do esgoto do estado de São Paulo é de 53,34% (Sistema Nacional de Informações sobre Saneamento, 2013). Uma possível explicação reside no fato de os investimentos em oferta de água potável serem

percebidos como prioritários comparados à coleta e tratamento de esgoto, tanto pela população quanto pelos governantes (Rydin et al., 2012).

Esgoto não tratado contribui para acúmulo excessivo de nutrientes nos corpos de água doce (eutrofização), e consequente proliferação de cianobactérias nos reservatórios de água (Cheung et al., 2013). As cianobactérias produzem metabólitos tóxicos para a saúde (ibidem), alguns reconhecidamente carcinogênicos, como a microcistina (IARC 2010). O meio ambiente também é prejudicado (morte de peixes, por exemplo), o que impacta também as atividades turísticas.

Segundo a Organização Mundial da Saúde, uma fonte de água potável segura é aquela protegida de contaminação externa, especialmente contaminação por fezes. Já uma infraestrutura de saneamento adequada é aquela que separa de forma higiênica os excrementos humanos do contato humano como vasos sanitários, sistemas de esgoto canalizado, fossas sépticas, vários tipos de latrinas e banheiros de compostagem (WHO; Unicef; 2014). No entanto a classificação errônea (classificar suprimento de água e esgoto como adequado, quando na verdade não atinge critérios básicos para tal) é frequente (Rydin et al., 2012); e fontes de fornecimento de água consideradas potáveis ainda podem conter contaminação por bactérias ou químicos (Dora et al., 2015).

Além disso, estima-se que os períodos de falta de água nas cidades se tornaram mais frequentes por causa das mudanças climáticas (Dora et al., 2015), ameaçando as conquistas no suprimento de água potável e saneamento alcançadas até o momento. Em 2015, o nível dos reservatórios de água da cidade de São Paulo caiu drasticamente. No começo do ano, a cidade enfrentou uma severa epidemia de dengue. As mudanças no fornecimento de água e o armazenamento inadequado de água da chuva em conjunto podem ter contribuído para o aumento nos casos de dengue em 2015.

Idealmente, todas as residências deveriam ter suprimento de água tratada para banheiros e cozinha, vasos sanitários e sistemas de drenagem de água da chuva para prevenir enchentes. No entanto essa realidade não atinge todos os residentes urbanos, particularmente os moradores de favelas (Rydin et al., 2012).

No Rio de Janeiro, 1,39 milhão de pessoas vivem em favelas. O acesso a água tratada e saneamento para essas populações é menor, comparado com os demais residentes da cidade (Snyder et al., 2013). O desafio de reduzir essa desigualdade é definir quem vai de fato pagar pela infraestrutura completa. A instalação de vasos sanitários dentro das residências costuma ser responsabilidade individual do morador e não das autoridades governamentais. Famílias de baixa renda, em especial aquelas que moram de aluguel em assentamentos informais, podem ter dificuldades em pagar por essa infraestrutura (Rydin et al., 2012).

Considerações finais

Os tópicos descritos separadamente neste artigo se sobrepõem sistematicamente aumentando a magnitude dos efeitos para a saúde das exposições

urbanas. Por exemplo, uma possibilidade de aumentar as áreas verdes discutidas no item "c" deste artigo é a promoção da agricultura urbana com implicações discutidas no item "b". Outra estratégia possível é o aumento do número de parques nas cidades.

Parques estão associados a um aumento no nível de atividade física, o que impacta positivamente a obesidade e outras doenças crônicas. Um estudo conduzido nos Estados Unidos entre 1993 e 1996 mostrou que crianças com acesso facilitado a parques e programas de recreação apresentavam menores índices de obesidade (Wolch et al., 2011). Também nos Estados Unidos, um estudo mostrou que comunidades de baixa renda têm acesso restrito a parques (ibidem). Além disso, os parques costumam ser mais poluídos em áreas de baixa renda (Su et al., 2011). Não é difícil imaginar que a situação no Brasil seja semelhante.

Neste artigo, propusemos uma discussão a partir dos cinco tópicos propostos por Rydin et al. (2012). No entanto, outras intervenções urbanas igualmente moldam a saúde nas cidades e não devem ser ignoradas. Por exemplo, um estudo conduzido por Epstein et al. (2012) mostrou que crianças que moram em bairros com menos lojas de conveniência e supermercados apresentam menor índice de obesidade.

A forma como as cidades funcionam influencia significativamente a saúde de seus moradores. Entender como se dá essa influência é um grande desafio metodológico, em razão das inúmeras variáveis envolvidas num sistema complexo como uma cidade. O uso de ferramentas metodológicas usadas para estudar sistemas é de grande valia no entendimento dos impactos do ambiente construído para a saúde. As evidências discutidas já oferecem direcionamentos sobre quais exposições presentes nos ambientes urbanos deveriam ser evitadas ou promovidas. Promover efetivamente as mudanças urbanísticas necessárias a uma cidade mais saudável requer a interação multidisciplinar entre diversas pastas do governo, a sociedade civil e outros atores da sociedade. Apesar da magnitude do desafio, o objetivo parece ser forte o suficiente para consensos efetivos, afinal uma cidade que promova a saúde de sua população é interesse de todos.

Ademais, uma cidade saudável deveria ser interesse particular dos profissionais de saúde, pois ela representa um grande auxílio terapêutico no enfrentamento de doenças e promoção da qualidade de vida.

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RESUMO – Morar próximo a um parque pode reduzir o risco de infarto do miocárdio, enquanto a exposição à poluição do ar ambiente aumenta o risco. Evidências associam a exposição crônica ao ruído do tráfego ao ganho de peso. Em 2014, mais de mil pessoas morreram no trânsito de São Paulo. No entanto, recomendar que as pessoas fiquem em casa com as janelas fechadas é inviável. A adoção de hábitos saudáveis é favorecida ou dificultada pelo ambiente construído e pelo modo como a cidade está organizada. Além disso, alguns fatores de risco para doenças, como a exposição à poluição do ar, vão além de escolhas individuais e dependem, em grande parte, de ações governamentais. Neste artigo discutimos os aspectos que podem favorecer ou dificultar a promoção da saúde nas cidades, a partir dos tópicos propostos por Rydin et al. (2012).

PALAVRAS-CHAVE: Saúde, Cidade, Ambiente construído, Políticas públicas.

ABSTRACT – Living near a park can reduce the risk for myocardial infarction, while exposure to outdoor air pollution increases it. There is evidence associating chronic exposure to traffic noise and weight gain. In 2014, more than one thousand people died in the São Paulo's traffic. However, recommending that people stay home with the windows closed is unfeasible. The adoption of healthy habits is aided or hindered by the man-made environment and by how the city is organized. Moreover, some risk factors for disease, such as exposure to air pollution, are beyond individual choices and call for governmental actions. In this paper, we discuss features that may aid or hinder the promotion of health in the city, based on a framework proposed by Rydin et al. (2012).

KEYWORDS: Health, City, Man-made environment, Public policies.

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4.4. 4. Artigo na revista Urbe

Urbe é uma revista brasileira de Gestão Urbana. Neste artigo[11], utilizei as evidências científicas da literatura para construir uma narrativa sobre cidades e qualidade de vida para urbanistas. Parte de uma edição especial sobre Urbanismo Ecológico publicada em 2015, a narrativa procurou estabelecer relações entre esta visão da arquitetura (urbanismo ecológico) e qualidade de vida, enfatizando que saúde ecológica e humana não são conceitos contraditórios, mas alinhados e poderiam ser usados em conjunto. A seguir apresento o artigo na íntegra.

How can ecological urbanism promote human health?

Como o urbanismo ecológico pode promover a saúde humana?

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Abstract

This special issue of URBE dedicated to Ecological Urbanism focuses on the role architects, landscape designers and urban planners can play in promoting healthier cities in Latin America. In this paper, we survey some of the empirical evidence that links the built environment with particular health outcomes. For many centuries, urban settlements were associated with adverse health outcomes, especially related to untreatable epidemics. As the science of disease transmission developed throughout the nineteenth century, the infrastructure of cities was transformed to promote improved public health. Significant gains were made, but in much of the world – Latin America included – urban health still remains a major challenge, all the more so as drug resistant strains of disease have become more prevalent. We believe Ecological Urbanism offers a promising framework for addressing these challenges. Distinguished by its integrated, multi-disciplinary foundation, Ecological Urbanism directly links both population and habitat health. This creates a natural opportunity for the design professions to play a more consequential role in shaping the health of urban settlements and, by extension, the regions they center.

Keywords: Urban health. Healthy cities. Ecological urbanism. Air pollution. Urban food production.

Resumo

Esta edição especial sobre urbanismo ecológico da revista Urbe destaca o esforço de arquitetos, urbanistas e designers em contribuir para cidades mais sustentáveis na América Latina. O objetivo deste estudo é oferecer aos arquitetos e urbanistas evidências científicas sobre como o meio ambiente urbano impacta a saúde. Historicamente, o viver nas cidades primeiro se associou com piores condições de saúde, representando um risco maior para cólera e doenças infecciosas. Depois das medidas sanitárias, viver nas cidades passou a

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ser uma vantagem para a saúde, quando comparado com a vida rural. Atualmente, a América Latina ainda convive com doenças infecciosas características do passado, ao mesmo tempo em que enfrenta um aumento crescente na incidência de doenças crônicas, classe de doenças que prevalecem na cidade e são modificadas pelo ambiente urbano. Com foco multidisciplinar e abordagem fluída entre diferentes escalas de análise, o Urbanismo Ecológico surge como uma solução promissora para proteger simultaneamente a saúde das pessoas e do planeta. Nós esperamos que, depois desta discussão, arquitetos e urbanistas usem a abordagem do Urbanismo Ecológico para abraçar a ideia de proteger a saúde através do exercício de suas profissões.

Palavras-chave: *Cidades saudáveis. Urbanismo ecológico. Mobilidade urbana. Poluição do ar. Agricultura urbana.*

Introduction

Changes in cities with the goal of increasing the energy efficiency of buildings, access to low-cost active transportation, and access to green spaces are key steps simultaneously to address climate change and to promote human health (Watts et al., 2015). Eighty percent of the population of Latin America (LA) live in urban areas, and inadequate or unplanned basic infrastructure remains a prevailing condition in many cities of this part of the world. Urban planners, architects and designers are in the position to reverse, or at least to mitigate, most of the unhealthy exposures characteristic of city environments, and the Ecological Urbanism (EU) approach offers a promising framework for addressing these challenges. Distinguished by its integrated, multi-disciplinary foundation, EU directly links population and habitat health, creating a natural opportunity for the design professions to play a more consequential role in shaping the health of urban settlements and, by extension, the regions in which they are centered.

In this paper, we aimed to provide architects and urban planners with empirical evidence about how city environments impact human health. Although there is a growing body of evidence relating city environments to human health, many questions remain unanswered due to the methodological challenges of addressing all of the variables of a complex system such as a city, as well as variability among local city realities. Furthermore, very robust scientific evidence is necessary to change practices linked to economic activities in complex scenarios. In a previous study, we showed that high local knowledge production in the field of air pollution was correlated with better local air quality at the national level (Fajersztajn, et al., 2013). Nawrot and colleagues (2011) showed that air pollution is an important trigger of myocardial infarction, similar in magnitude to other well-accepted risk factors (e.g., physical exertion and alcohol consumption), but the stringency of national air quality standards remains greatly different among countries (Vahlsing & Smith 2012). Scientists began to associate tobacco with severe health impacts in the early 50s (Doll & Hill, 1954), but important health-related polices were not implemented in some cities for a long time or were not implemented at all in other cities. Sao Paulo banned smoking in public spaces in 2009, other Brazilian cities banned it in 2014, but Havana has not banned it at all. Thousands of scientists at the IPCC (Intergovernmental Panel on Climate Change) endorsed the scientific evidence for climate change. However, we still do not have a global climate agreement. Without such robust scientific evidence, the international community would likely not be discussing a climate agreement at all (IPCC, 2013).

In this paper, we propose a discussion of the links between the built environment and public health from five thematic standpoints: a) transportation, mobility, and physical activity; b) urban food production; c) urban heat islands; d) thermal comfort and indoor air quality; and e) sanitation and wastewater management. Although we discuss these topics separately, there are overlaps between them. We classified the thematic areas according to Rydin et al. (2012) study because they discussed the role of urban planning in implementing health improvements from the perspective of health, which is our research field.

Despite the progress in the domains listed made over many decades, long before the term EU was coined, the resulting benefits were not experienced by all of the residents of LA cities. Furthermore, city environments are constantly changing (e.g., aging populations, new technologies, and climate change), requiring new and/or flexible approaches to urbanism

projects. Fluid in scale and with a disciplinary focus, EU has emerged as a promising framework to protect both the population and habitat health.

Nancy Krieger (2014) introduced the social determinants of health in the book *Ecological Urbanism*, and she showed that the neighborhoods of Boston affect health differently.

The Moving to Opportunity experiment conducted at Harvard University with 4,600 families showed that providing low-income families with assistance to move to better neighborhoods greatly improved the mental and physical health of children and adults (Ludwig et al., 2013; Chetty et al., 2015). If EU could reduce the socioeconomic disparities in a city, it would greatly benefit the health of urban populations in LA. Moreover, there are other forms in which EU can benefit human health. Some of the city-level polices to reduce greenhouse gas (GHG) emissions entail net benefits to human health (Watts et al., 2015).

Usually, different ecological approaches have argued against anthropocentrism because it has resulted in the unsustainable exploitation of nature resources and the related severe impacts on natural ecosystems. However, humans are not only aggressors but also victims, particularly regarding their own health. In Brazil, despite its effectiveness, the body of laws and regulations protecting ecosystems and biodiversity are robust, but the implications for the health of human beings due to changes in city environments are frequently neglected. While a new urban enterprise undergoes a strict environmental impact evaluation before being approved, possible health impacts, such as the adverse effects of noise and local air pollution exposure owing to changes in road use, are barely evaluated (Saldiva, 2010). It is important to emphasize that an ecological approach does not contrast with a human health approach.

The five domains we discuss in this paper are somewhat related to mental health, but considering the increased concern about mental illness in city environments, we will underscore some of these relationships. Although the potential influence of individual characteristics on mental health status is well recognized (WHO, 2014a), less is known about the association between features of the context in which an individual lives and their mental health (Weich et al., 2001). Studies have shown that greater socio-economic disadvantage, a poorer physical and social environment, and higher levels of crime are stressors that can lead to mental illness (Galea et al., 2011). A meta-analysis combined data from 16 countries and concluded that psychiatric disorders are more prevalent in urban areas – a 1.39 times higher risk – than in rural settlements (Peen et al., 2010). Mental and neurological disorders account for almost one quarter of the total burden of disease in LA and the Caribbean (PAHO, 2013). Rising levels of violence and mental illness in LA require integrated actions at the government level, as well as in health institutions, society, and other sectors (Harpham, 2009). Urban settlements could shape mental health for the better by reducing social deprivation and violence through the devices discussed in this paper (e.g., community gardens).

In this paper, we first briefly describe the historical links between health and urban planning. Next, we propose a discussion based on the five thematic areas proposed by Rydin et al. (2012): a) transportation, mobility, and physical activity; b) urban food production; c) urban heat islands; d) thermal comfort and indoor air quality; and e) sanitation and wastewater management. At the end of the paper, we present our final considerations, including further directions for research.

Urban planning and health: a historical overview

Public health and urban planning emerged with the common goal of reducing the harmful health effects of rapid industrialization and urbanization. Both fields were particularly concerned with preventing urban outbreaks of infectious disease (Corburn, 2004).

The first infrastructure improvements to promote better health in the early 19th century relied on miasma theory, which was the belief that diseases are caused by noxious substances present in bad-smelling air. This theory enhanced public concern with sanitation and hygiene. Engineering-based measures, such as sewers and garbage collection, contributed to containing disease in urban settlements. However, the great sanitary awakening came in the late 19th century, when the association between microorganisms and particular diseases were widely accepted, i.e., germ theory. Public health began to devise specific strategies for controlling and preventing specific diseases, based on laboratory identification of the

cause of the disease. At the same time, the public responsibility for health began to include not only environmental sanitation, but also individual health. Developing nations followed this trend, but they started the sanitary shift a few decades later, by the middle of the 20th century (Rydin et al., 2012). However, even now, sanitary facilities have not reached the entire urban population of LA, particularly the residents of slums, who are estimated to number 110 million people (FAO, 2014). In Sao Paulo, Brazil, the sanitary awakening started in the late 19th century, marked by the foundation of a company to supply residential water. However, sewage did not receive the same attention. The first law to regulate water pollution in the region was passed in 1940, and until today the sewage treatment rate for the state of Sao Paulo (of which the city of Sao Paulo is the capital) is 53,34% (Brasil, 2014). Access to health care facilities has played an important role in improving health outcomes in cities (Merzel, 2000), but they are not discussed in this paper.

During the sanitary reform, zoning in countries such as the United States embodied the concept of isolating urban populations from the undesirable externalities of the economy, and it separated the population from areas strictly designated for functions considered unhealthy, e.g., industry (Corburn, 2004). This model probably inspired some LA cities, but their major challenge has been unplanned growth and the continued expansion of slums and substandard housing. Basic urban infrastructure was not implemented at the same pace of the rapid growth of the urban population seen in LA.

Subsequently, urban planning and health aims moved in different directions. The main focus of city planning became enhancing economic outcomes. Public health focused on modifying individual risk factors (e.g., diet, exercise, and smoking), with successful outcomes. However, the health sector largely neglected the social dimensions of disease (Corburn, 2004), restricting the reach of health gains to selected populations.

Over the past few decades, the World Health Organization (WHO) has attempted to increase the overlaps between health and urban planning by two strategies – health in all polices (Ollila, 2011) and the healthy cities movement (Rydin et al., 2012) – but they are not yet robust in LA cities.

Recently, the health community has been concerned about the health impacts of climate change also increasing. In 2009, a series of papers published by *The Lancet* suggested that actions to reduce GHG emissions often, although not always, entail net benefits for health locally (Haines et al., 2009). This year, the same journal reported that tackling climate change could be the greatest global health opportunity of the 21st century (Dora et al., 2015; Watts et al., 2015). Because lower income populations are more vulnerable to climate change impacts on all scales, not only in comparing nations, but also within the same city, tackling climate change is an opportunity to reduce health inequalities. The EU approach discussed by Mostafavi & Doherty (2014), in their book that inspired this publication, is a golden opportunity to reinforce the links between public health and urban planning in LA cities, as well as links with the environment.

Building and maintaining cities that shape their residents' health for better are not simple tasks. According to the United Nations, 75.8% of the LA population live in 198 large cities, and 23% of urban residents live in slums without access to basic services, such as housing, clean water, and sanitation. Cities are complex systems, and WHO has recommended the use of trial and error in local projects to increase understanding of how best to improve urban health outcomes in specific contexts (Rydin et al., 2012). Hence, communication between city planners and the health sector should be improved and maintained, and this paper makes a contribution to the health discipline. To address this trial and error recommendation, we provide a broad variety of local examples.

In general, chronic non-transmissible diseases prevail in cities and are modified by them. The LA challenge is to face this modern pattern of diseases in highly urbanized regions, along with infectious diseases and widespread health inequality issues. The collaborative work between the health sector and urban planners might result in a considerable health gain for the region, particularly if planners focus on strategies to reduce the health inequalities within cities.

Historically, controlling the environment through technology (engineering-based measures) was the main concept driving the cooperation between the public health and urban planning fields, first through sanitary-based measures and then using a more sustainable design. Currently, architects and urban

planners seek alternative design approaches to address the whole infrastructure of cities in the EU. Some high income cities follow each step of this process. LA cities follow more flexible pathways because some of these cities are already implementing an EU approach, but they continue to struggle with poor sewage drainage and low-efficiency buildings.

Transportation, mobility, and physical activity

According to the WHO, transportation is one of the social determinants of health. However, its health aspects are not routinely addressed during the formulation and planning of urban transport polices in many LA cities (WHO, 2011).

The flow of goods and people within and through cities can negatively affect the health of people, the environment, and the economy. Therefore, there is an urgent need to improve transport in cities to address time and air pollutant emissions.

Currently, the urban environment in LA is frequently characterized by industrialization and environmental deterioration, as well as crowded cities surrounded by peri-urban poverty, traffic congestion, and few or low quality (comfort and time spending) public transportation options. The prevalent mode of transportation in cities is private cars. Moreover, having a car is synonymous with mobility, comfort, and status (Newman & Kenworthy, 1999). However, this mode of transportation results in serious health and environmental problems. Cars restrict physical exertion, contribute to isolation from social interaction and stress, and result in loss of hours from work and leisure due to time spent in traffic. Furthermore, cars contribute to air and noise pollution, negatively influencing health (Rissel, 2009). Additionally, car accidents kill thousands of people every year (Fletcher & McMichael, 1996 apud McMichael, 1996).

Hundreds of scientific studies have shown how transportation options can improve health status, prevent sedentarism-related diseases and mitigate harmful environmental impacts (e.g., greenhouse gases emission and urban air pollution). Environment-friendly and healthy alternatives include walking, cycling, and the use of public transportation. However, these alternatives must be safe, comfortable, accessible, inexpensive, convenient, efficient, and integrated to cover the whole city to stimulate their use, thus constituting a challenge for urban planners.

In Europe, strategies to create cycle networks and integration between cycling and public transportation have been successful, stimulating the use of active transport with significant environmental and health gains (Pucher & Buehler, 2008, 2007).

A recent systematic review of the health impacts of active transportation, conducted by Mueller et al. (2015), emphasized that active transport provides health benefits despite the risks of traffic accidents and exposure to air pollution, which are outweighed by the positive outcomes. Active forms of transportation are linked to increased physical activity and social interaction. Physical activity can improve the health status of an individual and can reduce the risk of developing several diseases, e.g., type 2 diabetes, hypertension, and obesity. Nevertheless, more than 30% of adults worldwide perform insufficient physical activity. Moreover, insufficient physical activity, together with a high-energy diet, is one of the causes of obesity. Active modes of travel can reduce the number of cars on the streets, thus benefiting the health by reducing air pollution.

Unlike in Europe and North America, fewer cities in LA have introduced active transportation initiatives. The recent review conducted by Moeller and colleagues did not find studies conducted in LA, but the authors excluded studies in Spanish and Portuguese Language. A search in the PubMed database (using the keywords "active transportation" and "physical activity") yielded 736 results but only four when the keyword "Latin America" was added. Moreover, only one (Becerra et al., 2013) study was in fact on the topic. According to Becerra and colleagues, the appeal for active transportation in LA is based on reducing traffic congestion and not on the environmental and health benefits of these strategies (Becerra et al., 2013). Ideally, both the health and environmental sectors should participate in the decision-making process, and urban planners should be aware of the impacts of a built environment and transportation modes on health.

In contrast, the Web sites of South American cities depict initiatives in Sao Paulo, Rio de Janeiro, Curitiba, Bogotá, Buenos Aires, and Santiago. The World Bank has also published reports on the successful implementation of BRT (bus-based rapid transit) systems in different countries (e.g., Ecuador, Mexico). Initiatives that stimulate active transport also include the construction of exclusive bike lanes

and the closure of streets to motorized traffic during the weekends and on holidays for cycling, running, and walking. Evaluation of the health benefits of these initiatives has been rare, and the methods to estimate or predict their health impacts are not precise. Laverty et al. (2015) examined the correlations among socio-demographic status, the use of active travel, and specific health outcomes (adiposity, diabetes, blood pressure) in adults (mean age: 58 years old) from six middle-income countries: Mexico, China, India, South Africa, Russia, and Ghana. They found that people who use more active modes of transport presented a reduced risk of being overweight and lower systolic blood pressure and BMI (body mass index). Saunders et al. (2013) noted that active travel could have positive effects on health outcomes but not specifically on obesity.

Thus, active transportation not only reduces urban traffic, air pollution, and climate-associated changes, but it also improves the health status of people. The benefits rely on healthy increases in physical activity and social interaction, and on reducing the levels of air-pollutant exposure in urban areas, which constitutes a major environmental risk factor for cardiovascular disease and lung cancer. The only way to reduce air pollution exposure is to reduce ambient levels, which requires reducing the emission of pollutants. According to the WHO (2014b), in 2012, there were 58,000 premature deaths in LA due to air pollution exposure.

Vehicle fleets contribute the most to GHG emissions and therefore to climate change, as well as increased mortality owing to extreme temperatures. The impact of temperature on health will be discussed in the "Urban heat islands" section of this paper.

Active transport integrated into an efficient public transportation system is an alternative to improve human health, reduce environmental pollution, and mitigate climate change. The challenge that urban planners and policy makers face today in developing counties is how to implement these changes in previously built urban environments designed to favor the private car mode of transport and to attract users.

Urban food production

Despite the widespread notion of food production as an exclusively rural activity, the growing of plants and raising of animals within and around cities (FAO, 2014) are not new occurrences. Food insecurity due to poverty (Zezza & Tasciotti, 2010; Wolch et al., 2014), war (Milburn & Vail, 2010; Rydin et al., 2012), and natural disasters (Hara et al., 2013) has assured the occurrence of the activity in past decades. At present, UPA (Urban and Peri-urban Agriculture) is also reemerging in the more sustainable cities of developed nations (Middle et al., 2014; Hara et al., 2013; Rydin et al., 2012).

It is not possible to project that UPA will replace traditional forms of feeding in highly populated cities, but the potential benefits for ecology and human health cannot be ignored. The WHO appealed to cities and their governments to incorporate food policies into urban plans (Rydin et al., 2012).

UPA is widespread in LA. In Rosario, Argentina, 1.35 million inhabitants have 800 community gardens producing vegetables for 40,000 people (FAO, 2014). In Mexico City, nearly 23 thousand ha of land are dedicated to crop production, and in Cuba agriculture is practiced by 40 thousand urban workers on an estimated area of 33,500 ha (FAO, 2014).

The benefits of urban food production range from improvements in health and social outcomes to environmental and economic benefits. UPA is good for health because it improves human nutrition. Compared with other urban dwellers, urban producer families have more diverse diets and consume more vegetables and fruits (FAO, 2014). Low ingestion of vegetables and fruits is a major risk factor for the global burden of disease (Lim et al., 2012). In LA and the Caribbean, low intake of whole grains and other nutrition-related risks are also among the top ten major risk factors for disease. Better nutrition benefits cardiovascular health (Hu et al., 2001) and helps to combat other non-communicable diseases, such as obesity (Gatto et al., 2015) and diabetes (Tohill et al., 2004). UPA also creates opportunities for physical activity, reinforcing the described health gains (Rydin et al., 2012). Furthermore, engaging in urban food production potentially enhances emotional health through stress reduction and socialization. Along with improving access to quality food, UPA has proved to be an important response to anticipated food shortages due to natural disasters, droughts, and increases in food prices, among other situations (Hara et al., 2013; Rydin et al., 2012; Angnotti, 2015).

The services to the ecosystem from agriculture include the regulation of water and climate systems,

maintenance of soil fertility, and the regulation of pollination, among others (Swinton et al., 2007). When food is locally produced, there is a reduction in transportation demand, resulting in energy savings and a decrease in the emissions of air pollutants (Angnotti, 2015; Hara et al., 2013), all of which are ecological gains. Other potential gains include reduction in solid waste exporting due to composting projects (FAO, 2014) and better management of rainwater through wider urban green coverage, which also allows for groundwater restoration (Angnotti, 2015).

UPA contributes to economic growth through employment and other forms of income generation because families engaged in UPA reduce their spending on food and earn additional income from sales (FAO, 2014). Revitalization of low-income communities (Angnotti, 2015) and the raising of the value of local housing due to the amelioration of landscape aesthetics (Rydin et al., 2012) might emerge as indirect social and economic gains. Security is enhanced by greater civic involvement and the presence of more people outside in yards and gardens (Rydin et al., 2012), which also promote social cohesion (FAO, 2014).

The agro-ecological approach enhances environmental and nutritional gains (Baranski et al., 2014) and perfectly suits EU values because both concepts share integrative views of environmental sustainability. Furthermore, the agro-ecological approach might be cost-effective in specific settings. In Havana, producing 1 million tons of vegetables via organic agriculture is US$39.5 million less expensive than conventional agriculture (FAO, 2014).

Despite its particular challenges, the city is an appropriate venue for integrating food production with other ecosystem services (FAO, 2014). Even in densely populated areas, food can be produced in containers on rooftops and balconies, in parks and elsewhere. It is important to note that food production in the city is possible, but replacing the current forms of food supply to feed cities is not yet possible, and it is not currently a goal at all. UPA should ideally occur alongside the current forms of food supply, and EU might be an appropriate approach for UPA and other forms of food supply to cities coexisting.

The dominant form of urban food production in LA is backyard family horticulture and school gardens, but the region also has other forms of community and commercial gardens. UPA production includes the farming of vegetables, fruits, and cereals, the raising of small animals for eggs and meat, and the growing of flowers. All age groups and walks of life are engaged in these activities, but most of them come from low-income households. Women are the more prevalent gender, particularly in the Caribbean, Bolivia, Colombia, Ecuador, Honduras, and Nicaragua (FAO, 2014). In El Alto, Bolivia, a gardening project taught more than one thousand families production techniques adapted to the city's agro-climatic conditions. The result is that, in one year, a typical family produces nearly 1 ton of tomatoes, saves US$60 a month on food purchases, and earns US$15 from the sale of surpluses (FAO, 2014).

UPA is under increasing pressure from urbanization itself. A major issue is the lack of space, resulting in the high cost of land and competitive use. In the peri-urban area of Rosario, Argentina, soybeans for export have displaced other traditional produce for the domestic market, such as wheat, sunflowers, milk, and fruit. In Mexico City and Lima, slums and industrial activity have been impairing water quality and availability for agriculture use (FAO, 2014). Technical issues can be overcome, but most cities must still face the lack of quality seed, the poor quality of soils, and the unreliability of water supplies (FAO, 2014). There is also the need to overcome UPA-related trade issues, including the high cost of inputs and the unavailability of credit to buy tools and processing equipment; very limited access to markets is also a major issue (FAO, 2014; Angnotti, 2015). Moreover, the overuse of agrochemicals exposes some small farmers to health risks and impairs environmental quality, polluting water supplies and other natural resources (FAO, 2014).

Finally, we draw attention to the role of contaminated soil in urban areas, which often contains dangerous levels of heavy metals (Cheng et al., 2011; Ferri et al., 2015). Heavy metals are present in the soil of many urban vegetable gardens in the United States and Europe (Clark et al., 2008; Cheng et al., 2011; Burt et al., 2014; Ferri, et al., 2015), prompting questions about the potential health consequences of UPA in contaminated areas.

Lead and other heavy metals have been strongly linked to severe cognitive, motor and behavioral disorders in children (Grandjean & Landrigan, 2006). Researchers agree that the exposure routes for humans occur through accidental ingestion of the soil and inhaling of contaminated dust (Kessler, 2013), posing

risks to farmers, particularly children. There is less consensus about the health effects of the consumption of crops grown in contaminated soil (Warming et al., 2015; Ferri et al., 2015; Augustsson et al., 2015), probably due to the general lack of studies, particularly in LA. The broad range of variables involved – soil constitution, type of pollutant, type of crop – has impaired comparisons between studies. Hence, the most prudent attitude is to follow the specific management practices for urban gardeners (Kessler, 2013), which can help to prevent these harmful exposures. Some of these recommendations are closely related to urban planners' activities, such as building gardens away from existing roads.

More successful UPA in LA cities has received technical support from international organizations and/or NGOs. Political will has also played a role. Cities where local UPA was successful also inspired national policies, spreading UPA across the country, as occurred in Nicaragua and Honduras (FAO, 2014).

Enhancing UPA requires support from all levels of government because it should be integrated with activities from different levels of governance, such as solid waste management, water supply, and education. In LA, 12 countries have implemented national policies promoting UPA (FAO, 2014).

Many LA cities use composting for urban organic waste fertilizer (FAO, 2014). The region also has experience in better managing of water, storing rainwater, reusing resources, and using technologies that conserve water. In El Alto, new technologies have reduced by 80% the need for water by crops (FAO, 2014). There has also been successful experience with converting pig manure into biogas and selling the energy to urban residents (FAO, 2014). In general, all schools, parks, and community facilities are candidates for composting projects and for growing food (Angnotti, 2015).

Zoning urban areas for agriculture can protect against competition with other land uses and can facilitate the recognition of UPA as an economic activity. However, zoning usually neglects UPA (Rydin et al., 2012); only three nations in LA have explicitly included it in their occupation planning (FAO, 2014). Furthermore, protecting sustainable agriculture by small-scale farmers in peri-urban agriculture by law could safeguard water reservoirs (FAO, 2014).

Before choosing an area for UPA, it is recommended that the local conditions (soil, light incidence, water supply, etc.) be evaluated. In the absence of contaminant tests (the gold standard), the local history of urbanization and industrialization has indirectly addressed the potential contamination of the soil. In cases of previous industrial activities, gas stations, and laundry services, it is prudent to consider the soil contaminated. Remediation is frequently possible, but the unavailability of specialized services at some sites and the high costs might be impediments. Building raised beds and importing healthy soil are alternatives (Rydin et al., 2012; Angnotti, 2015; Kessler, 2013). Kessler (2013) summarized the best management practices for urban gardeners, including agricultural practices (e.g., covering existing soil and walkways with mulch) and good habits (e.g., wearing gloves).

Financial-related mechanisms, such as heavily taxing vacant land and providing credits for urban farming, can play key roles in overcoming the high cost of land (Angnotti, 2015).

Architects and designers have already developed solutions to cope with the lack of space for activity; vertical farms, including rooftop crops, are an example (Torreggiani et al., 2012).

Specific polices can address technical issues with UPA, such as lack of quality seed, poor quality of soils, and the unreliability of water supplies. The same is true for trade-related issues, such as the high cost of inputs, the unavailability of credit for equipment, and lack of access to markets. Experiences in LA have shown that trading production with schools and hospitals and promoting technologies that add value to UPA production enhance the activity. In Antigua and Barbuda, fruit drinks and sun-dried hot peppers from backyard gardens are improving the financial gains of gardeners (FAO, 2014).

Occupational health risks owing to the overuse of agrochemicals can be prevented by the agro-ecological approach, which is also aligned with ecological values. In some countries, the use of synthetic pesticides and fertilizers is forbidden by law.

Finally, urban planners and designers can incorporate UPA concepts while planning new buildings and cities. In China, some buildings have been planned with level rooftop surfaces that can be used for farming. The arrangement improves the solar angle for natural lighting within apartment buildings, as well as natural cross-ventilation (Rydin et al., 2012).

Urban heat island

The accelerated urbanization rate is changing the landscape and soil coverage. Buildings, roads, and other infrastructure have replaced land and vegetation, resulting in elevated temperatures in urban areas, compared to their outlying rural surroundings, which is a phenomenon known as urban heat islands (Berdahl & Bretz, 1997; Sobral, 2005).

The magnitude of surface Urban Heat Islands (UHIs) varies by the season, due to changes in the sun's intensity, ground cover, and weather. Atmospheric UHIs are often weak during the late morning and throughout the day and become more pronounced after sunset due to the slow release of heat from the urban infrastructure. The timing of this peak depends on the properties of urban and rural surfaces, the season, and prevailing weather conditions (Akbari, 2005). Increased daytime surface temperatures, reduced nighttime cooling, and higher air pollution levels associated with UHIs can affect human health by contributing to general discomfort, respiratory difficulties, heat cramps and exhaustion, non-fatal heat stroke, and heat-related mortality. UHI can also exacerbate the impact of heat waves, which are periods of abnormal heat. Sensitive people, children, the elderly, and those with chronic diseases are at major risk. The Centers for Disease Control and Prevention estimated that, from 1979 to 1999, excessive heat exposure contributed to more than 8,000 premature deaths in the United States (CDC, 2004).

Urban pollution contributes to complex atmospheric processes (Akbari, 2005; EPA, 2006); hence, the emission of pollutant gases must be considered when analyzing the meteorological variables of large cities (Coelho et al., 2010).

In Sao Paulo, the thermal gradient between the outskirts and the central zone can reach 10 °C. The reduction of green coverage, the increased use of fossil fuels, and the construction of high buildings that act as ventilation barriers can explain UHIs (Sobral, 2005). In addition, modifications of the urban thermal profile affect sensible heat, latent heat and momentum fluxes, surface convergence, optical properties of the atmosphere, boundary-layer height, and other boundary-layer features. Such changes impact pollution dispersion, thunderstorm initiation, and many other physical and chemical processes in the urban environment (Khan & Simpson, 2001).

Despite the broad variety of meteorological systems that affect Sao Paulo, the city presents two well-defined seasons: Spring-Summer (hot and wet) and Fall-Winter (cold and dry) (CDC, 2004), but extreme weather events intensified by climate change are becoming more frequent (Bornstein & Lin, 2000). In winter, pollutant concentrations can be critical because of the low availability of solar energy, limiting the development of the planetary boundary layer. Hence, pollution dispersion is heavily dependent on the strength of the heat island circulation (Bornstein & Lin, 2000). The health consequences are increasing hospital admissions due to cardiorespiratory diseases (Coelho et al., 2010; Braga et al., 2002; Saldiva et al., 1992), and sometimes death (WHO, 2004). UHIs also increase ground-level formation of ozone, which is a pollutant related to acute asthma crises (Andrade et al., 2004). Nitrogen and volatile organic compounds, which are released from fossil fuel combustion, react in the presence of sunlight, forming ozone, particularly during the high temperature periods of late spring and early autumn (Hsieh et al., 1999; Andrade et al., 2004). Further, the temperature gradient between central (hot) and peripheral areas (less hot) of the city from UHIs increase heavy rain events in the central part of the city (Freitas et al., 2007). Urban effects can be particularly important for explaining the daily rainfall extremes in the summer (Silva Dias et al., 2013), leading to floods and associated health problems (leptospirosis infections).

Thermal pollution can aggravate respiratory and cardiovascular diseases (WHO, 2004; Guo et al., 2014; Laschewski & Jendritzky, 2002), and it is associated with discomfort and physiological stress. The thermal comfort neutrality range falls between 17 °C and 31 °C. Above that temperature, hypotension, hyperthermia, tachycardia, heart failure, poor appetite, dehydration, fatigue, irritability, decreased learning ability, impaired memory, and depression may occur. An increase in air temperature also impacts flora and fauna, influencing the distribution of vector-borne diseases, such as dengue fever (Coelho & Massad, 2012; Laschewski & Jendritzky, 2002).

Moreover, changes in meteorological parameters in large cities due to urbanization and global warming have affected weather in these places. As a result, heat waves, dry weather, and rain are very likely to increase in both frequency and intensity. In urban regions, these future heat waves will be exacerbated by the UHI effect

and will have the potential to influence negatively the health and welfare of residents. In Shanghai, China, a study showed that UHIs are directly responsible for adverse health effects due to exposure to extreme thermal conditions (Tan et al., 2010). Socioeconomic factors modulate the health burden of temperature extremes (Urban et al., 2014; Burkart et al., 2011). Temperature and mortality are usually associated. In England and Wales, a study analyzed 10 areas during the summer from 1993 to 2006, and heat was associated with increased mortality in nearly all causes of death in the elderly (Gasparrini et al., 2012).

Weather event extremes present a significant health risk, and the hazard is likely to escalate with the increased future temperatures presently predicted by climate change models. The impact of heatwaves is often stronger in densely populated cities and where the climate is involuntarily modified to produce an UHI effect.

Humans have mechanisms for managing additional heat and cold, but overcoming this vital threshold can lead to serious health conditions. A recent study published in *The Lancet* with 384 locations in 13 counties revealed that uncomfortable ambient temperature is responsible for considerable increases in mortality, with significant differences between countries. According to the results, the temperature is responsible for increasing a considerable proportion of deaths to 7.71% (95% CI 7.43-7.91). Nevertheless, there are significant inter-country variations in attributable risk (for both hot and cold), with the uppermost attributable risk in Italy, China, and Japan and the lowermost estimates in Thailand, Brazil, and Sweden (Gasparrini et al., 2015).

Health impacts and vulnerability due to extreme weather events require systematic approaches and integrated policy and planning responses from a range of government agencies. Unfortunately, effective mitigation actions are almost non-existent in Brazil. According to Marengo et al. (2009), by 2100, the average temperature may have risen between 2 °C and 4 °C in Brazil, compared with the average temperatures recorded between 1961 and 1990. Thermal discomfort conditions will affect thousands of people. There will likely be an increase in the number and severity of cases of heart disease, asthma and infections. At a higher level of severity, individuals who use medication chronically to control respiratory and heart diseases will require higher doses to control their illnesses to cope with environmental changes. Increased susceptibility to pollutants and climatic factors is dependent on individual, environmental and socioeconomic factors and on housing conditions (Souza & Macedo, 2010).

In contrast, developed countries have implemented significant mitigation policies in urban planning, with a focus on sustainability and energy but that indirectly have co-benefits to health. For example, Green Infrastructure (GI) has contributed to the mitigation of UHIs. In the context of climate change, with the expected increase in temperature, the dryness and intensity of heat waves, and storms and floods, green areas assume even greater importance because they can create a cooling effect that extends to surrounding areas.

The project of the Urbanism, Climate Adaptation and Health Cluster, funded by the CSIRO Climate Adaptation Flagship, focuses on improving understanding of the interactions between climate and health in urban areas in Australia, using green infrastructure (GI) to address high temperatures and dry humidity (CRC, 2012).

A European commission has produced guides to assist authorities and stakeholders in investing in Green Infrastructure (GI) through the Cohesion Fund for 2014-2020. The first is a guide to "*multi-benefit cohesion policy investments in nature and green infrastructure*" (European Commission, 2015).

Seven federal agencies have united to support the Green Infrastructure Collaborative in the United States of America. These agencies signed a *Federal Letter of Support* committing to specific actions to promote green infrastructure. The cooperating agencies are the EPA, the Department of Housing and Urban Development, the Department of Transportation, the Department of Agriculture, the Department of the Interior, the Department of Defense, and the Department of Energy (EPA, 2014).

Implementation of UHI mitigation strategies, such as increased vegetative cover and higher-albedo surface materials, was suggested by studies performed in New Jersey addressing issues such as economic efficiency and the reduction of energy consumption and costs at the sites (Solecki et al., 2005). Urban food production, previously discussed in this paper, might be an option for vegetative cover.

Finally, interventions can be implemented at various levels: urban planning, with the implementation of climate controlling factors, such as afforestation, squares, streets, policies to decrease emissions from pollutants, etc.; and housing, with improvements in the constructive conditions that favor thermal insulation to protect residents (more information in the "Thermal comfort and indoor air quality" section).

A third level of intervention is education: educational campaigns and awareness of the adverse effects of weather and orientation of attitudes could facilitate protection against cold/heat or pollution (Sobral, 2005; CDC, 2004).

Thermal comfort and indoor air quality

Urban planners, architects, and designers can help to assure better indoor quality and thermal comfort for urban inhabitants at home, work, school or other facilities. The major challenge will be how to improve indoor environments for the 110 million slum dwellers in LA (2010) (FAO, 2014).

Indoor air pollution is among the top risk factors for chronic diseases in LA (Lim et al., 2012), and it was responsible for 7% of the premature deaths in the region (WHO, 2014b) in 2010. Indoor air quality is modulated by air exchange, outdoor pollutant levels, and the production of indoor pollutants (Rydin et al., 2012). Architects are in the position to improve air exchange and consequently indoor air quality.

The burning of solid fuels for cooking and heating is the most studied source of indoor air pollution. The impacts on health include increased risks of pneumonia in children (<5 years old) and of chronic obstructive pulmonary disease, cardiovascular disease, cataracts, and lung cancer in adults (Smith et al., 2013). Women and small children are the most vulnerable because they spend the most time in or near the kitchen. The lack of access to clean energy sources can also result in other health risks, such as burns, injuries, intoxication, and violence against women while they collect fuel (Dora et al., 2015).

In Brazil, the highest percentage of a population in a metropolitan region without a stove at home was 1.76% in Fortaleza (IBGE, 2011). However, this percentage could be significantly higher in the less-developed countries of LA (Laborde et al., 2015). More efficient biomass stoves (ideally attaining nearly complete combustion) have been a successful solution. In Guatemala, child pneumonia decreased by half in houses that successfully (90% reduction in the levels of indoor air pollutants) installed wood stoves with chimneys (Smith et al., 2011). Additionally, improved cooking stoves reduce GHG emissions, both benefiting public health and mitigating climate change (Wilkinson et al., 2009). Affordable household electricity would also result in better indoor air quality because the use of gas or electricity to cook creates little or no pollution in the kitchen (Smith et al., 2013). However, improving household ventilation is an important mitigation strategy, and architects and designers must be aware of it.

Similarly, improved insulation, efficiency of heating and the use of other building materials that reduce heat losses through the walls, windows, and roof are among the successful strategies to reduce energy use (Rydin et al., 2012).

Warmth and energy efficiency interventions can improve general health, particularly in people with previous chronic respiratory diseases (Thomson et al., 2013). Furthermore, thermal comfort strategies are likely to improve cardiovascular health because low indoor temperature is associated with a higher risk of high blood pressure (Shiue & Shiue, 2014)

Indoor tobacco smoke is also a recognized source of indoor air pollutants (Laumbach & Kipen, 2014). Restricting smoking indoors is an effective police for reducing exposure (Sebrié et al., 2008), but it is probably beyond the abilities of urban planners. However, improving ventilation can also help mitigate exposure to indoor tobacco smoke.

Asbestos is a carcinogenic substance (IARC, 2009) related to a wide variety of lung diseases (O'Reilly et al., 2007), including asbestosis, a disease caused by the inhalation of asbestos (Bledsoe et al., 2014). Due to its insulating, fire-resisting and sound-absorbing properties, asbestos was usually mixed with cement for building construction materials, particularly roofing products (Haynes, 2010). Asbestos is virtually banned in most developed countries (Laborde et al., 2015). In LA, Argentina, Chile, Uruguay and Honduras have also banned asbestos (Laborde et al., 2015). In the other countries, if possible, architects and designers should avoid using building materials with asbestos and other noxious compounds (e.g., formaldehyde) in their composition to improve indoor air quality (Wang & Zhang, 2009).

Sanitation and wastewater management

Safe drinking water access and sanitation are basic human rights (UN, 2010). There is widespread understanding that the lack of access to safe drinking water, sanitation, and hygiene affects human health (WHO/UNICEF, 2014), particularly causing diarrheal outbreaks. Malnutrition, vector-born disease (e.g., dengue fever), neglected tropical diseases (e.g., schistosomiasis), and non-communicable disease risks related to chemical contaminants are recognized health outcomes (Freeman et al., 2013; Bartram et al., 2005). Poor people are at greater risk because their access to improved water sources and sanitation is restricted (Dora et al., 2015)

In LA and the Caribbean, the access to safe drinking water reached 94% of the population in 2012. The lowest levels of coverage were found in the Dominican Republic, Ecuador, Haiti, Nicaragua and Peru, ranging from 76% to 90% (WHO/UNICEF, 2014).

The scenario is worse for improved sanitation facilities. In 2012, 110 million people in the region still lacked access to sanitation, despite improvements in previous years (WHO/UNICEF, 2014). One explanation is that investment in infrastructure to supply water tends to be seen as a priority by politicians and citizens, whereas the disposal of human excreta is comparatively neglected (Rydin et al., 2012).

According to the WHO/UNIFEC Joint Monitoring Program for Water Supply and Sanitation, an improved drinking-water source is protected from outside contamination, in particular from contamination with fecal matter, and should include: piped water into dwellings; piped water to yards/plots; public taps or standpipes; tubewells or boreholes; protected dug wells; protected springs; and rainwater (WHO/UNICEF /JMP). An improved sanitation facility is one that hygienically separates human excreta from human contact: flush toilets, piped sewer systems, septic tanks, flushing/pouring to pit latrines, ventilated improved pit latrines, pit latrines with slabs and composting toilets. Flushing/pouring to outside, pit latrines without slabs, buckets, hanging toilets or hanging latrine, and a lack of facilities or bushes or fields are classified as unimproved sanitation facilities (WHO/UNICEF, 2015). However, many unimproved systems might be misclassified, (Rydin et al., 2012) and improved drinking water sources might still contain substantial bacterial and chemical contamination (Dora et al., 2015).

In addition, climate change is expected to increase the risk of water shortages in urban areas (Dora et al., 2015), threatening the achievements of water and sanitation facilities. In 2015, the water sources of the city of Sao Paulo decreased drastically, impairing the water supply. At the beginning of the year, the city also faced a severe dengue fever epidemic. Inadequate rainwater collection and water storage are possible causes of the increase in dengue fever cases in 2015.

Ideally, all households should have a potable water supply for internal bathrooms and kitchens, a flushing toilet, and storm drainage to prevent flooding, but in many cities, this set of standards can only be achieved in the wealthiest neighborhoods. Informal settlements are of particular concern (Rydin et al., 2012). In Rio de Janeiro, Brazil, people living in informal settlements (1.39 million people) have less access to adequate water and sanitation, compared with the other residents of the city (Snyder et al., 2014). Urban planning regarding sanitation must focus on reducing unequal access. A major challenge is defining who will pay for it. Usually, city authorities see on-site toilet facilities as the responsibility of individuals. Poor houses in informal settlements are unlikely to have financial capital invested in such facilities, particularly those living in rental properties (Rydin et al., 2012).

A recent report described a step-by-step approach to the complex circumstances surrounding the need to provide sanitation to urban areas, particularly to densely populated areas and to the less affluent sectors of society. It considered financial issues, as well as other dimensions, institutional, environmental, technical and social (Galli et al., 2014).

Considering all of the dimensions, increasing the effectiveness of sanitation measures results in health protection for those that received these facilities. However, if city planners also consider the concepts of ecological urbanism, the environment would also be protected. In addition, the ecological urbanism approach is a tool for integrating the planning of green areas and sanitation, both of which are essential for the environment and human health. The "Urban heat islands" and "Urban food and agriculture" sections discussed some of the wide variety of benefits to green spaces.

Final considerations

Ecological and human health gains in city environments are not at odds. Distinguished by its integrated and multi-disciplinary foundation, EU is an opportunity to promote population and habitat health and to reduce health inequalities in LA, a part of the world where 80% of population lives in cities, 23% of it in slums.

The empirical evidence discussed in this paper shows that urbanism-related measures can shape human health for better or worse. Experiences from developed (more abundant) and LA cities can inspire the use of trial and error in local projects in LA to increase understanding of how best to improve urban population and habitat health, applying an EU approach in specific urban contexts.

Similar to initiatives that have proposed indicators linking health and sustainability for the post-2015 development agenda, a next step to enhance the links between EU and population health could be the proposal of health indicators that shape human health for better city environments.

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5. DISCUSSÃO

Trabalhando no terceiro setor eu almejava contribuir para a promoção de uma cidade mais saudável. Ao longo do tempo percebi que as relações entre urbanidade e qualidade de vida eram demasiadamente complexas e vi na ciência um instrumento que poderia me auxiliar a compreender melhor essas relações. Ingressei na pós-graduação com a expectativa de dominar algumas técnicas científicas, de ser capaz de produzir pesquisa independente, de integrar conhecimentos científicos e resultados complexos e criar artigos de qualidade para reportar o conhecimento produzido. Mais que isso, eu queria entender como a ciência pensa e ao mesmo tempo desenvolver habilidades de tradução dos achados científicos em narrativas compreensíveis para um público mais geral. Embora esse processo de aprendizado terá que ser desenvolvido continuamente ao longo da vida, sinto que o ingresso na pós-graduação foi positivo para que eu começasse a desenvolver essas habilidades.

Nos resultados desta tese apresentei minha experiência com oito manuscritos, em formatos diversos e para públicos variados, sete deles de alguma forma já publicados[10,11,25,53,56–58] e o oitavo já submetido. A preparação dos manuscritos seguiu um processo dinâmico, onde o aprendizado com cada artigo resultou em novas habilidades e perguntas de pesquisa. Por exemplo, o primeiro estudo (tipologia 1, poluição do ar e câncer)[53], influenciou os demais, tanto no que diz respeito a gerar novas perguntas de pesquisa, quanto no que diz respeito a forma de construção da narrativa. A pergunta do manuscrito da tipologia 2[57], "qual a cobertura de monitoramento de poluição do ar em países em desenvolvimento?" surgiu a partir de constatações feitas durante o primeiro estudo. São elas: a) estudos sobre poluição do ar e saúde são relativamente escassos em países em desenvolvimento comparado com

países desenvolvidos; b) a contribuição de evidências produzidas em países em desenvolvimento é escassa em análises globais sobre poluição do ar e saúde como as conduzidas pelo IARC*. Cenário semelhante (ausência de estudos associando material particulado fino e eventos diários de saúde) contribuiu para a formulação da pergunta de pesquisa da revisão sistemática (tipologia 3). Mapear dados secundários como estratégia de construção de narrativas também foi usado no capítulo de livro sobre poluição do ar e reprodução humana(58) (tipologia 4) e na construção do índice de defasagem tecnológica(56) (manuscrito sobre co-benefícios para a saúde de políticas de baixo carbono, tipologia 1). Transcender o tema poluição do ar e trabalhar com outros temas relacionados a urbanidade e qualidade de vida, indica que avancei na análise de temas complexos, como me propus inicialmente. Os manuscritos incluídos na tipologia 4, demonstram que foi possível produzir artigos que integrem diferentes áreas de conhecimento sob a forma de narrativas compreensíveis para um público mais amplo. Cada um dos quatro manuscritos desta tipologia foi publicado num veículo voltado para públicos diversos, como urbanistas no caso da Revista Urbe(11) e gestores públicos no caso da revista Estudos Avançados(10). Acredito que este resultado permite afirmar que é possível produzir artigos científicos de bom nível que, ao mesmo tempo integrem diferentes áreas de conhecimento e orientem formadores de opinião, gestores públicos e órgãos legislativos desejosos de estimular políticas voltadas para a promoção da saúde e qualidade de vida, como perguntado no objetivo desta tese.

Ao longo da pós-graduação participei ainda de outros estudos não mencionados na sessão de Resultados, um deles finalizado, mas ainda não publicado. Trata-se de uma contribuição sobre as relações entre saúde humana e crise hídrica para um dossiê sobre a

* IARC corresponde à sigla em inglês que designa a Agência Internacional de Pesquisa sobre Câncer, vinculada à Organização Mundial da Saúde.

crise hídrica de São Paulo. Intitulado o livro Branco da Água, o dossiê reuniu cientistas de diversas áreas sob a coordenação da Academia de Ciências do Estado de São Paulo e do Instituto de Estudos Avançados (IEA) da Universidade de São Paulo e visa atingir especialistas e tomadores de decisão. O dossiê será publicado em breve e pode ser acessado na seção de Anexos desta tese (Anexo C). Ter sido solicitada para escrever sobre água e saúde, indica que as habilidades que desenvolvi ao longo da pós-graduação podem ser utilizadas para abordar outros temas do guarda-chuva saúde e urbanidade.

Quando transferi minha pós-graduação do mestrado para o doutorado direto, acordei com meu orientador que eu aprenderia técnicas de revisão sistemática e metanálise, o que fiz através de uma especialização. A especialização resultou num manuscrito já submetido (vide seção de Resultados) e num segundo baseado na mesma pergunta de pesquisa, mas para o poluente MP_{10}*, ao invés do $MP_{2.5}$† e está em processo de preparação. Uma nova pergunta de pesquisa surgiu a partir desta revisão sistemática e será investigada através de um *overview*‡ (vide registro do protocolo da pesquisa na seção de Anexos, Anexo D). O aprendizado sobre revisão sistemática aprimorou minhas habilidades em procurar, selecionar, avaliar a qualidade e sintetizar evidências científicas e as tenho também utilizado na condução de revisões não sistemáticas. De fato, tenho uma certa fluência no tema, a ponto de ministrar aulas sobre o assunto em outras Faculdades e ter sido convidada para participar de uma revisão sobre exposição gestacional à poluição do ar e desenvolvimento pulmonar, em curso neste momento.

Assim como aconteceu nos objetivos, métodos e resultados, as discussões correspondentes a cada um dos manuscritos que compõe esta tese está contida no corpo

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* Tipo de poluente atmosférico definido por seu tamanho, no caso do MP_{10}, material particulado com diâmetro aerodinâmico menor que 10 micrômetros.

† Tipo de poluente atmosférico definido por seu tamanho, no caso do $MP_{2.5}$, material particulado com diâmetro aerodinâmico menor que 2.5 micrômetros.

‡ O termo em inglês "*overview*" é usado pelos teóricos em revisão sistemáticas e ainda não possui tradução para o português. Refere-se a revisões de revisões sistemáticas.

dos mesmos (vide seção de Resultados). Deste modo vou me dedicar a discutir aspectos mais gerais e conceituais que não puderam ser transformados em artigos, mas que de alguma forma indicam a minha transformação ao longo da pós-graduação.

Em primeiro lugar, convenci-me ainda mais que o tema urbanidade e qualidade de vida é complexo. As cidades não são fáceis de gerir, cada intervenção acarreta uma série de efeitos na cidade, nem sempre previsíveis ou desejáveis[31].

Políticas baseadas em evidência são um instrumento valioso para gerir as cidades[47,48,59]. Prevenir exposições ambientais que a ciência mostrou serem tóxicas[55,60–63], reduzir inequidades em saúde[61–65] e melhorar a eficiência dos gastos públicos são apenas alguns dos benefícios potenciais de política públicas baseadas em evidência. Ademais, politicas baseadas em evidência aprimoram a qualidade e a legitimidade das democracias[47].

Informar políticas públicas tem sido tema cada vez mais central da agenda científica[64]. Ao longo das últimas décadas, a comunidade científica tem desenvolvido uma série de estratégias metodológicas para diminuir a distância entre política e evidência, notadamente técnicas de revisão sistemática[60,66,67] e metodologias de avaliação da qualidade da evidência, desenvolvidas e aplicadas não só por algumas revisões sistemáticas[60,68], mas também por grupos maiores de pesquisadores e especialistas, como Sociedades Médicas e organizações internacionais e multiprofissionais como o IARC* e o IPCC†. No campo da saúde, os pesquisadores tem sido cada vez mais desafiados a mostrar que estão impactando políticas públicas e ajudando a reduzir a distância entre evidência e política, tanto por alguns pré-requisitos

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† IPCC corresponde à sigla em inglês que designa o Painel Intergovernamental sobre Mudanças Climáticas composto por centenas de cientistas qualificados e vinculado a Organização Mundial de Meteorologia e ao Programa das Nações Unidas para o Meio Ambiente.

de financiamento, quanto por alguns pré-requisitos de publicação. No entanto, a transformação do conhecimento científico em melhores decisões políticas não ocorre de forma natural[48]. Não basta produzir ciência de qualidade, é também preciso apresentá-la de uma forma compreensível para um público mais abrangente, particularmente gestores públicos, órgãos legislativos e formadores de opinião, o que dentro da teoria de produção de políticas públicas é chamado de transferência do conhecimento[48]. Estratégias de melhor tradução do conhecimento são de fato fundamentais[69]. A função do pesquisador é produzir ciência no mais alto nível de qualidade possível, mas não necessariamente traduzi-la. São exceções os cientistas que também produzem boas narrativas sobre suas pesquisas. Para traduzir ciência é preciso entender sobre ciência e sobre o público receptor, o que não é uma tarefa fácil. Para traduzir a ciência é preciso se equilibrar entre uma narrativa responsável, que defina acertos e limitações das conclusões, sem se prender na incerteza, característica inerente do linguajar científico. Embora não tenha sido o objetivo deste estudo, percebi que o que a sociedade quer saber é se a poluição dá ou não câncer, se determinada fonte de água é segura ou não para beber e outras definições que os métodos científicos que utilizamos nem sempre nos permitem afirmar. Como já mencionado, a qualificação das evidências científicas é e deve continuar a ser feita por organizações que desenvolveram metodologias e critérios específicos para isso e ainda contam com a colaboração de diversos cientistas e especialistas com diferentes formações para avaliar o conjunto de evidências, como ocorre no IARC[*] e IPCC[†]. No entanto, a construção cuidadosa de uma boa narrativa também pode ajudar a interlocução entre ciência e os interessados nos seus achados,

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incluindo pesquisadores de outras áreas. Uma das contribuições notáveis da Faculdade de Saúde Pública de Harvard é o boletim informativo[*], onde eles transformam uma série de estudos moleculares e com metodologias complexas numa narrativa compreensível para a população em geral. Os pesquisadores da Harvard em si permanecem comprometidos com a produção do melhor conhecimento possível e a Universidade, como política interna, coloca este conhecimento disponível para a população.

Segundo Choi[48], a produção de políticas baseadas em evidência envolve gerar, transferir e incorporar conhecimento e o sucesso de uma determinada política depende da contemplação de todas essas etapas. Neste estudo, pude experimentar principalmente estratégias que Choi[48] classifica como pertencentes à etapa de transferência do conhecimento. As estratégias sugeridas pelo autor para aprimorar a transferência do conhecimento são: a) produção de conteúdo relevante, b) tradução apropriada, c) *timing*[†] e d) novos métodos de organizar e publicar a informação prioritária. Os manuscritos que compõe essa tese de certa forma abrangeram todas as estratégias sugeridas, exceto a última.

Convenci-me ainda mais que não basta produzir ciência de qualidade e apresentá-la de uma forma compreensível para um público mais abrangente, é preciso integrar os conhecimentos científicos de diversas áreas numa mesma narrativa. Ou seja, frente a complexidade das relações entre urbanidade e qualidade de vida, não basta a narrativa de um setor, é preciso integrar o conhecimento em narrativas, mas também integrar as diversas narrativas. É este o ponto ao qual me referi na introdução desta tese, quando disse que a saúde saiu da caixa da saúde. É justamente a integração de diversas

[*] O boletim é geralmente enviado por e-mail, mas também pode ser acessado pelo website: http://www.health.harvard.edu/.

[†] *Timing* em português pode ser entendido como um momento extremamente oportuno e favorável para a divulgação de uma determinada informação, considerando contextos sociais mais amplos, como por exemplo a publicação do artigo sobre poluição e câncer[53] no momento em que se discutia se o câncer era carcinogênico para humanos.

narrativas que tem o potencial de fazer frente ao desafio de gerir cidades que promovam a qualidade de vida de seus habitantes. Ainda há muitas perguntas sobre como essa integração poderia ocorrer mais efetivamente. Há pesquisadores que desencorajam a integração de conhecimentos científicos produzidos a partir de teorias conceituais diferentes[(70)]. Outros, apontam caminhos como o uso de abordagens sistêmicas[(71)], mas as sugestões ainda se restringem quase que exclusivamente ao campo teórico.

Recentemente a Universidade de São Paulo (USP) lançou um Programa que pretende mostrar possíveis caminhos para integrar narrativas de diversos setores e, em última análise, devolver a sociedade o conhecimento produzido dentro da Universidade. Hospedado no Instituto de Estudos Avançados da Universidade de São Paulo[*], o Programa USP Cidades Globais esta desenvolvendo uma metodologia para utilizar os recursos intelectuais da USP para integrar o conhecimento de forma a prover meios para que São Paulo atinja o mais alto nível como cidade global[†]. Coordenado pelo prof. Marcos Buckeridge, a metodologia inicial foi inspirada na teoria de redes complexas e visa identificar propriedades emergentes, entendidas pelo Programa como as relações entre as diversas áreas do conhecimento produzido na USP sobre cidades. Algumas das relações entre disciplinas diversas do conhecimento já são conhecidas e podem ser potencializadas. Além disso, relações antes ocultas podem emergir a partir da integração de diferentes áreas do conhecimento. A partir destas relações, o Programa pretende construir uma narrativa conjunta, guiada pelo objetivo comum de melhorar a qualidade de vida e o bem-estar dos habitantes de São Paulo. A visão do Programa é aumentar a qualidade de vida e bem-estar dos paulistanos e quem sabe implementar um instituto de cidades globais na USP no futuro. Lançado para o público geral em julho de 2016, faço

[*] O Instituto de Estudos Avençados da Universidade de São Paulo é atualmente presidido pelo meu orientador, Prof. Paulo Saldiva, um dos idealizadores do Programa USP Cidades Globais.
[†] Cidade Globais são aquelas que mais influenciam o mundo conforme cinco domínios: negócios, capital humano, troca de informações, experiência cultural e engajamento político [(78)].

parte da coordenadoria executiva do Programa, onde pretendo desenvolver melhor habilidades de integração de narrativas envolvendo o complexo sistema urbanidade e qualidade de vida. A visão do Programa está de acordo com um entendimento da importância de valores na gestão das cidades, também advogado por um grupo de cientistas através de um movimento chamado "*Planetary Health*"*[34].

Na prática, o sucesso de uma política baseada em evidências pode envolver outros aspectos não abordados por Choi[48]. Ademais, as políticas públicas nem sempre são guiadas por valores como uma melhor qualidade de vida para o maior número de pessoas possível. Por exemplo, no caso do controle da poluição do ar, políticas baseadas em evidência têm sido muitas vezes adiadas nos países em desenvolvimento[72], em virtude de um aparente dilema entre crescimento econômico e proteção da saúde humana e ambiental, acarretando na perda de benefícios potenciais para a saúde da população e para o meio ambiente, já extensivamente demonstrados[73]. A concepção de que é preciso crescer primeiro para só depois controlar a poluição ambiental, surgiu na década de 90, com base em observações temporais do desempenho econômico e ambiental de países que, de forma geral, obedeciam a uma curva de U invertido, conhecida como curva de Kuznets[49,50,74,75]. A corrente que defende que economia e desempenho ambiental não são variáveis necessariamente acopladas, que o desempenho ambiental depende de outros fatores[50,75] e que a poluição não melhora com a melhora da economia, mas sim a partir da adoção rigorosa de políticas públicas de controle[49] são menos ouvidas no Brasil e em outros países em desenvolvimento. Possivelmente isso ocorre mais em virtude da disputa de interesses econômicos na sociedade, do que pela qualidade da evidência científica apresentada pelo segundo grupo, indicando uma

* Além da série de artigos publicados no The Lancet, o grupo de cientistas publicou um manifesto no mesmo jornal que atingiu mais de sete mil assinaturas: http://www.thelancet.com/manifesto/planetary-health.

predominância de valores econômicos, em detrimento de valores diretamente relacionados com a qualidade de vida da maioria da população.

Falhar, adiar ou demorar para tomar ações baseadas em evidência não é uma escolha política neutra ou livre de consequências[60] e pode privar a população de usufruir benefícios para saúde já apontados pela ciência[60,73]. No mundo todo é preciso diminuir o tempo discorrido entre a descoberta científica e seus benefícios para a saúde[60,76,77], em especial em nações em desenvolvimento, onde a distância costuma ser maior. No entanto há diversos grupos de interesse na sociedade, todos merecedores de voz, o que potencializa a dificuldade de gerir as cidades. Neste contexto, no meu entendimento, e também de meu orientador, a decisão política deveria ser baseada por valores que passam pela compreensão de qual é o bem maior. Entendemos que a qualidade de vida e a dignidade humana da grande maioria da população poderia ser o valor norteador de todas as políticas urbanas. Este valor está alinhado com o que outros cientistas que estudam meio ambiente e qualidade de vida tem proposto em âmbito internacional[35]. O Programa USP Cidades Globais pode ser um instrumento importante para verificar possibilidades da aplicação desses valores na prática. Ademais, se considerarmos a teoria de sistemas complexos e propriedades emergentes proposta pelo Programa para melhorar a qualidade de vida dos paulistanos, citada anteriormente nesta discussão, a inclusão de direitos humanos como um valor orientador de políticas públicas foi uma propriedade emergente que surgiu do conjunto de artigos que compões esta tese.

6. CONCLUSÃO

A partir dos oito manuscritos apresentados nesta tese, concluímos que é possível produzir artigos científicos de bom nível* que, ao mesmo tempo, integrem diferentes áreas de conhecimento e orientem formadores de opinião, gestores públicos e órgãos legislativos desejosos de estimular políticas voltadas para a promoção da saúde e qualidade de vida.

* Definidos para fins deste estudo como aqueles publicados em periódicos que utilizam análise por pares.

7. ANEXOS

Anexo A.

Aprovação do Comitê de Ética em Pesquisa da Faculdade de Medicina da Universidade de São Paulo.

MEDICINA

USP

COMITÊ DE ÉTICA EM PESQUISA

APROVAÇÃO

O Comitê de Ética em Pesquisa da Faculdade de Medicina da Universidade de São Paulo, em sessão de 06/06/2012, APROVOU o Protocolo de Pesquisa nº 162/12 intitulado: "ESTUDO DA POLUIÇÃO ATMOSFÉRICA NO MUNDO A PARTIR DA RELAÇÃO ENTRE CONCENTRAÇÃO GLOBAL DE MATERIAL PARTICULADO, PRODUTO INTERNO BRUTO PER CAPITA, PRODUÇÃO CIENTÍFICA SOBRE POLUIÇÃO ATMOSFÉRICA E DIVULGAÇÃO DO CONHECIMENTO CIENTÍFICO SOBRE POLUIÇÃO ATMOSFÉRICA." apresentado pelo Departamento de PATOLOGIA

Cabe ao pesquisador elaborar e apresentar ao CEP-FMUSP, os relatórios parciais e final sobre a pesquisa (Resolução do Conselho Nacional de Saúde nº 196, de 10/10/1996, inciso IX.2, letra "c").

Pesquisador (a) Responsável: Paulo Hilário Nascimento Saldiva
Pesquisador (a) Executante: Laís Fajersztajn

CEP-FMUSP, 12 de Junho de 2012.

Prof. Dr. Roger Chammas
Coordenador
Comitê de Ética em Pesquisa

Comitê de Ética em Pesquisa da Faculdade de Medicina
e-mail: cep.fmusp@hcnet.usp.br

Anexo B.

Material suplementar referente ao artigo de revisão sistemática em processo de submissão apresentado na seção de resultados (Seção de Resultados, item 4.3)

Supplemental Material

Short-term effects of $PM_{2.5}$ on daily health events in Latin America: a systematic review and meta-analysis.

Laís Fajersztajn, Paulo Saldiva, Luiz Alberto Amador Pereira, Victor Figueiredo Leite, Anna Maria Buehler

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S2. Studies excluded by reason……...

S3. Association measurements conversion procedures ……..

S4. References…….

S1. Search strategy

Search strategy used at Pubmed, Scopus, Web of Science, Cochrane and Embase databases:

((("Air Pollution"[Mesh] OR Air Pollution OR Air Pollutions OR Pollution, Air OR Pollutions, Air OR "Particulate Matter"[Mesh] OR Airborne Particulate Matter OR Particulate Matter, Airborne OR Air Pollutants, Particulate OR Particulate Air Pollutants OR Pollutants, Particulate Air OR Ambient Particulate

Matter OR Particulate Matter, Ambient OR PM 10)) AND ("Latin America"[Mesh] OR Latin America OR Argentina OR Barbados OR Belize OR Bolivia OR Brazil OR Chile OR Colombia OR Costa Rica OR Cuba OR Dominican Republic OR Ecuador OR El Salvador OR Guatemala OR Guyana OR Haiti OR Honduras OR Jamaica OR Mexico Or Nicaragua OR Panama OR Paraguay OR Peru OR Suriname OR Trinidad and Tobago OR Uruguay OR Venezuela))) AND ("Hospitalization"[Mesh] OR Hospitalization* OR hospital admission* OR emergency room visit* OR "Mortality"[Mesh] OR Mortality)

Search strategy used at Lilacs database:

Search included Decs (Health Sciences Descriptors) terms and was performed in English, Portuguese and Spanish languages, as described below:

(tw:(poluição do ar OR contaminación del aire OR air pollution)) OR (tw: material particulado OR MP10 OR particulate matter)) AND (tw: (mortalidade OR mortalidad OR mortality OR hospitalization OR admissão hospitalar OR admisión hospitalar OR emergency room visits OR emergência OR emergencia)) AND (instance:"regional")

S2. Studies excluded of the review by reason.

Did not meet eligibility criteria (n=153)		
Study design and period evaluated (n=36)		
Amancio et al. 2012	Duchiade 1992	Paraiso and Gouveia 2015
Anenberg et al. 2011	Filleul et al. 2001	Silva et al. 2012
Avendaño C et al. 1999	Garcia-Reynoso et al. 2007	Prieto et al. 2007
Avendaño C et al. 2003	Goncalves et al. 2005	Ribeiro and Cardoso 2003
Bell et al. 2011	Hernández-Cadena et al. 2007	Riguera et al. 2011
Botter et al. 2002	Mascarenhas et al. 2008	Rosa et al. 2008
Bueno et al. 2010	Castro and Neria 2003	Silva et al. 2010
Carneseca et al. 2012	Muñoz et al. 2009	Silva and Ribeiro 2012
Castro et al. 2007	Nascimento and Medeiros	Silva et al. 2014
Castro et al. 2010		Steven et al. 2008

Chang et al. 2004	2012	Telez-Rojo et al. 2001
Cifuentes et al. 2001	Nicolella and Belluzzo 2015	Coutinho et al. 2015
Duchiade and Beltrao 1992	Oliveira et al. 2012	
Exposure characteristics (n=62)		
Adamkiewicz et al. 2001	Freitas et al. 2004	Nardocci et al. 2013
Alencar and Santos 2014	Daumas et al. 2004	Nascimento et al. 2006
Amancio and Nascimento 2012	Diaz-Robles et al. 2015	Nascimento et al. 2012
Amancio and Nascimento 2014	Gavinier and Nascimento 2014	Nascimento and Francisco 2013
Amarillo and Carreras 2012	Gouveia and Fletcher 2000a	Negrisoli and Nascimento 2013
Andrade Filho et al. 2013	Gouveia and Fletcher 2000b	O'Neill et al. 2006
Arbex et al. 2000	Gouveia et al. 2006	O'Neill et al. 2004
Arbex et al. 2007	Gurjar et al. 2010	O'Neill et al. 2008
Arbex et al. 2009	Habermann and Gouveia 2012	Ostro et al. 1996
Arbex et al. 2010	Hernández-Cadena et al. 2000	Pinheiro et al. 2014
Arbex et al. 2014	Hernández-Cadena et al. 2007	Romero-Placeres et al. 2004
Bakonyi et al. 2004	Ignotti et al. 2010	Romieu et al. 2004
Bell et al. 2006	Lin et al. 1999	Romieu et al. 2012
Blanco-Becerra et al. 2014b	Lin et al. 2003	Saldiva et al. 1994
BorjaAburto et al. 1997	Mardones et al. 2015	Saldiva et al. 1995
Braga et al. 2001	Martins et al. 2002a	Sanhueza et al. 2006
Braga et al. 2007	Martins et al. 2002b	Sanhueza et al. 2009
Bravo and Bell 2011	Melgar-Paniagua et al. 2013	Santos et al. 2008
Cançado et al. 2006	Moura et al. 2009	Souza et al. 2014
Carbajal-Arroyo et al. 2011	Naumova et al. 2007	Tellez-Rojo et al. 1997
Conceicao et al. 2001		
Farhat et al. 2005		
Outcome characteristics (n=15)		
Barbosa et al. 2015	Diaz-Robles et al. 2014	Sousa et al. 2012a
Cakmak et al. 2010	Lin et al. 2004	Vera et al. 2007
Carmo et al. 2010	Ostro et al. 1999	Vera et al. 2008
Dales et al. 2009	Pereira et al. 1998	Zamorano et al. 2003
Dales et al. 2012	Pereira Filho et al. 2008	
Population characteristics (n=4)		
Darrow et al. 2011	Gittins et al. 2013	Murray and Lipfert 2012
Galan et al. 2003		
Association measure characteristics (n=33)		
Blanco-Becerra et al. 2014a	Franck et al. 2014	Moura et al. 2008
Braga et al. 1999	Ghement et al. 2007	Nascimento 2011
Cakmak et al. 2007	Gonçalves et al. 2007	Nunes et al. 2013
Cakmak et al. 2009b	Gouveia et al. 2003	Oliveira et al. 2011
Cakmak et al. 2009a	Grass and Cane 2008	Reyna et al. 2013
Cakmak et al. 2011	Gutierrez 2015	Romero-Lankao et al. 2013
Carmo et al. 2013	Jasinski et al. 2011	Salinas and Vega 1995
Cendon et al. 2006	Ilabaca et al. 1999	Sousa et al. 2012b
Cifuentes et al. 2000	Leiva et. Al 2013	Tellez-Rojo et al. 2000
Cook et al. 1998	Martins et al. 2004	Vera and Cifuentes 2009
Franck et al. 2015	Martins et al. 2006	Yanagi et al. 2012
Studies which aim was to evaluate the effect of temperature (n=3)		
Carreras et al. 2015	O'Neill et al. 2005	Sharovsky et al. 2004

Full text could not be retrieved (n=5)		
Giraldo 2008	Penna and Duchiade 1991b	Target and Cabanes 2005
Penna and Duchiade 1991a	Sanhueza et al. 2008	
Duplicates (conference papers published as a full paper retrieved by the search) (n=3)		
Freitas et al. 2001	Martins et al. 2001	Tellez-Rojo et al. 1999
Overlap of populations (n=1)		
Castillegos et al. 2000		

S3. Association measurements conversion procedures

RR= (RPC/100)+1

RR=((exp(ß x vp)

ß = LnRR/vp

e = (ln (upper CI) - (ß x vp))/1,96 x vp

where RR is the relative risk, ß is the coefficient regression, vp is the variation in pollutant concentration, e is the error and CI is the Confidence Interval

S4. References

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Anexo C.

Manuscrito preparado para o Livro Branco da Água. Ainda não publicado.

Crise hídrica em São Paulo e saúde

Laís Fajersztajn e Paulo Saldiva

A rápida expansão da mancha urbana na região metropolitana de São Paulo resultou em alterações do microclima da região, agravadas pelas mudanças climáticas. Antes conhecida como terra da garoa, a região convive atualmente com períodos alternados de seca e chuvas intensas que impactam significativamente a saúde de seus moradores e impõe novos desafios para a proteção da saúde pública. Embora por motivos divergentes, doenças de veiculação hídrica reemergem em taxas elevadas durante a cheia e a seca, ameaçando conquistas importantes da saúde pública, como a queda da mortalidade infantil por diarreia. Ainda, determinados contaminantes presentes na água para consumo humano ameaçam a saúde para além das conhecidas diarreias e outras doenças infecciosas, e estão cada vez mais relacionados ao câncer e outras doenças crônicas. Proteger a população das doenças de veiculação hídrica impostas pelo ambiente urbano atual é um desafio interdisciplinar que requer esforços que vão além das competências tradicionalmente atribuídas ao setor de saúde. Por exemplo, no Brasil, o Ministério do Meio Ambiente regulamenta a qualidade do ar, águas e solo e o Ministério da Saúde regulamenta a qualidade da água para consumo humano (Umbuzeiro, 2015). Como discutiremos adiante, a qualidade da água dos reservatórios influencia significativamente a qualidade da água que chega às torneiras, de modo que o diálogo entre as pastas é fundamental para um melhor desempenho da saúde coletiva. O mesmo vale para outras disciplinas do conhecimento e escalas de governo. O desafio atual de promoção da saúde pública passa necessariamente pelo desafio da gestão integrada e efetiva de conhecimentos.

No caso dos recursos hídricos, o arcabouço legal já aponta na direção da gestão integrada, mas a prática ainda apresenta muitos desafios. Em conformidade com discussões internacionais, a gestão integrada e descentralizada dos recursos hídricos já é reconhecida por lei no Brasil. Apesar do pioneirismo do estado de São Paulo em promulgar uma política integrada e descentralizada dos Recursos Hídricos em

1991[*] (a política nacional em moldes similares é de 1997) [†], a efetividade prática deste prática deste modelo tem sido criticada, particularmente durante a crise hídrica do estado iniciada em 2012 e intensificada no verão de 2013/2014. Em artigo recente publicado na revista "Estudos Avançados", Jacobi e colaboradores (2015) apontaram falhas do governo do Estado de São Paulo em integrar a sociedade na discussão das soluções para o enfrentamento da crise hídrica na região, reforçadas por falhas na cobertura da mídia. O artigo pode servir como referência para entender parte do arcabouço legal (incluindo descrição das Bacias Hidrográficas da região) e práticas administrativas da gestão dos recursos hídricos no Estado de São Paulo.

Valentim (2015) deixa clara a preocupação do setor de saúde com a evolução contínua do conceito de potabilidade frente aos novos conhecimentos científicos e às modificações dinâmicas do cenário onde se dá a produção da água (bacia hidrográfica). Ele destaca os Planos de Segurança da Água-artigo 13 da Portaria Federal vigente (MS 2914/2011)- como o grande avanço legal, pois vão além da potabilidade e das características físicas e operacionais do sistema ou solução alternativa, e incluem controle e vigilância da qualidade da água desde o manancial até o consumidor. No entanto, ao fazer recomendações para o estabelecimento efetivo dos Planos de Segurança da Água, Valentim (2015) acaba por revelar que, apesar dos esforços, na prática a gestão dos recursos hídricos ainda não está de fato integrada. Embora ressalte a importância da discussão para avanços futuros, Valentim (2015) relata o insucesso de uma discussão ocorrida em 2008 entre diversas secretarias estaduais (Saúde, Meio Ambiente, Recursos Hídricos e Saneamento e Agricultura e Abastecimento) em estabelecer dispositivos legais regulamentadores para uma gestão pública integrada de segurança da água de consumo humano em São Paulo.

A crise hídrica vivenciada em São Paulo a partir, principalmente, do verão 2013/2014, parece evidenciar uma crise de integração de conhecimentos traduzida numa dificuldade real de gestão integrada dos recursos hídricos, exemplificada tanto por Valentim (2015), quanto por Jacobi e colaboradores (2015). A proteção da saúde pública frente às exposições impostas pela crise hídrica de São Paulo vai depender da difícil tarefa de integrar conhecimentos diversos, produzidos a partir de gramáticas diversas. Nossa proposta é uma leitura do cenário hídrico de São Paulo numa

[*] Política Estadual de Recursos Hídricos, Lei n.7.663, promulgada em 1991
[†] Política Nacional de Recursos Hídricos, Lei n.9.433, promulgada em 1997

perspectiva de saúde. É possível, e na verdade desejável, que outros textos sejam mais eficientes em explicar pormenores das interações ambientais, legislação a cerca da gestão dos recursos hídricos e respostas técnicas. O nosso objetivo é dar uma perspectiva ampliada dos aspectos da gestão hídrica relacionados à saúde, para além dos já reconhecidos padrões de potabilidade. Primeiro, discutiremos os desafios da qualidade da água para consumo humano impostos pelo período de seca. Abordaremos os possíveis impactos para a saúde originados pela deficiência nos sistemas de distribuição de água e pelo aumento da poluição dos reservatórios. A estiagem diminui a capacidade de diluição dos poluentes dos reservatórios, aumentando a poluição dos mesmos. As possíveis consequências exploradas neste artigo são o aumento dos contaminantes químicos na água pelo maior uso de produtos para tratamento da água e a proliferação de cianobactérias com resíduos tóxicos nos reservatórios de água. Também discutiremos consequências para a saúde do possível aumento de uso de fontes de água mais poluídas e de fontes não controladas. A figura 1 exemplifica as possíveis relações entre estiagem e saúde. Em seguida, discutiremos aspectos das mudanças no microclima regional, com ênfase nas ilhas urbanas de calor. A primeira vista pouco relacionada com a estiagem, à alteração no microclima regional auxilia no entendimento mais amplo da crise hídrica, para além da situação atual, porque traz a perspectiva de como o estilo de vida urbano impacta na saúde do meio ambiente, que nos fornece a água, e na saúde humana. Por fim, para enfrentar o cenário atual, sugerimos que esforços integrados de saberes, como os propostos nesta publicação, sejam orientados sob o objetivo comum de proteger a saúde coletiva.

1. Qualidade da água para consumo humano

O principal impacto para a saúde humana da estiagem na cidade de São Paulo é seu potencial comprometimento da qualidade da água. Superadas através de medidas sanitárias bem sucedidas, as doenças infecciosas de veiculação hídrica tendem a reemergir com algumas especificidades características do contexto atual, incluindo a possível emergência de doenças crônicas. Dentre as doenças infecciosas de veiculação hídrica, vale destacar a diarreia. Responsável por desconforto e limitação momentânea, a consequente desidratação causada pela diarreia pode ter impactos devastadores em grupos vulneráveis como crianças e idosos. Em 2013, 57,8 mil crianças menores de cinco anos morreram no mundo como consequência da diarreia, em geral originadas por

problemas de qualidade da água (Liu et al., 2015). Em países em desenvolvimento, a ocorrência de episódios frequentes de diarreia na infância tem sido cada vez mais relacionada com prejuízos no crescimento e desenvolvimento cognitivo das crianças. O prejuízo em longo prazo iria além da saúde pública nacional, prejudicando o desempenho da economia, por perda de capital humano. O mecanismo por trás dessa associação seria a relação entre a infecção gastrointestinal e a desnutrição, condição reconhecidamente associada ao prejuízo do desenvolvimento infantil. A inflamação decorrente da diarreia prejudicaria a absorção de nutrientes. Haveria também perda de proteínas. Ambos resultando em má nutrição. A desnutrição por sua vez, prejudicaria a resposta inerente do sistema digestivo, exacerbando a gravidade da infecção e impulsionando um ciclo vicioso (Maclntyre et al., 2014).

1.1.Deficiências no sistema de distribuição

O período de estiagem em São Paulo veio acompanhado de relatos de intermitência e baixa pressão nos sistemas de distribuição de água. Ambas as condições estão entre as deficiências de distribuição de água reconhecidamente associadas a surtos de doenças de veiculação hídrica (Lee & Schwab 2005), em particular diarreia. A interrupção da distribuição de água em redes de distribuição contínua favorece a contaminação externa da água do sistema, desde que haja deficiências na integridade do encanamento, o que pode resultar em aumento da incidência de infecção do trato intestinal. Embora haja heterogeneidade significativa entre os estudos, uma metánalise recente (Ercumen et al., 2014), mostrou que o risco de aumento combinado (quatro estudos) na incidência de infecção do trato intestinal durante períodos de interrupção na distribuição de água pode ser 3,26 vezes maior comparado com períodos de operação normal do mesmo sistema.

Relatos de jornal, baseados em dados do Centro de Vigilância Epidemiológica do Estado de São Paulo, mostram que em 2014, ano de estiagem, o estado registrou 315 mil casos de diarreia. O pico ocorreu em fevereiro, quando foram observados 70% mais casos de diarreia que a média esperada (35 mil contra 20 mil casos). Além das interrupções no abastecimento e da baixa pressão no sistema, os jornais também apontam a origem da água (uso do volume morto das represas e de água de poços e caminhões pipa) como possíveis causas da epidemia de diarreia no estado (Felix 2015; Martín 2015). De fato, a contaminação na fonte também configura uma deficiência no sistema de abastecimento de água relacionada a surtos de diarreia (Ercumen et al., 2014).

1.2.Aumento da poluição dos reservatórios

Durante períodos de estiagem, a qualidade da água dos reservatórios fica prejudicada, pois há menos água para diluir os poluentes presentes nas fontes remanescentes. Além disso, passa-se a considerar o uso de fontes com qualidade inferior, que não estavam sendo utilizadas anteriormente. Ambas as situações exigem o uso de processos químicos mais agressivos para garantir a potabilidade da água, aumentando a formação de um grupo de contaminantes orgânicos conhecidos pela terminologia em inglês "desinfection by-products", os DBPs. Mais de 700 componentes químicos já foram identificados como DBPs (Villanueva et al., 2014). Os DBPs são gerados a partir da reação química entre matéria orgânica e desinfetante usada para reduzir os microrganismos patogênicos da água, como cloro e ozônio. Presentes na água para consumo humano e também em piscinas de uso recreativo, os DBPs têm sido consistentemente associados com alterações no desenvolvimento e na reprodução humana, além de estarem relacionados com o surgimento de câncer, particularmente câncer de bexiga (Richardson & Ternes, 2014).

Se por um lado o tratamento adequado da água para consumo humano diminuiu significativamente as doenças infecciosas por contaminação microbiológica, o aumento da poluição dos reservatórios de água impõe um novo risco de saúde para a população por aumentarem a poluição da água de consumo humano por DBPs. Em recente revisão, Villanueva & colaboradores (2014) listaram recomendações para estudos epidemiológicos futuros sobre químicos presentes na água, tópico ainda pouco estudado, em parte por dificuldades metodológicas. Os autores destacam a necessidade de estudar os químicos emergentes, substâncias para as quais não há regulamentação sobre concentrações de segurança, mesmo em países desenvolvidos.

Por fim, a estiagem aumenta o uso de fontes alternativas de água, como poços e carro pipa, para as quais o controle de qualidade da água é menos frequente ou inexistente. O uso de fontes de água não tratada aumenta o risco de doenças de veiculação hídrica - em especial infecções entéricas, para as quais já há métodos conhecidos e efetivos de prevenção.

A atividade humana (esgoto, detergente e outros) tem resultado no acúmulo excessivo de nutrientes nos corpos de água doce (eutrofização), aumentando a ocorrência e a intensidade de cianobactérias nos reservatórios de água (Pantelic et al., 2013), alterando gosto e coloração da água. O excesso de nutrientes (principalmente

nitrogênio e fósforo), calor (acima de 20°C), luz solar e água parada criam condições favoráveis para a proliferação de cianobactérias (Cheung, et al, 2013). O fenômeno altera o ecossistema aquático com prejuízos significativos para a saúde humana e para a economia. A diminuição do oxigênio na água, em última análise, resulta na morte de peixes e a redução da atividade turística nas regiões afetadas impacta a economia. O custo anual da eutrofização dos corpos de água doce nos Estados Unidos pode superar $2.2 bilhões de dólares (Cheung et al., 2013). Não encontramos evidências para o custo no Brasil.

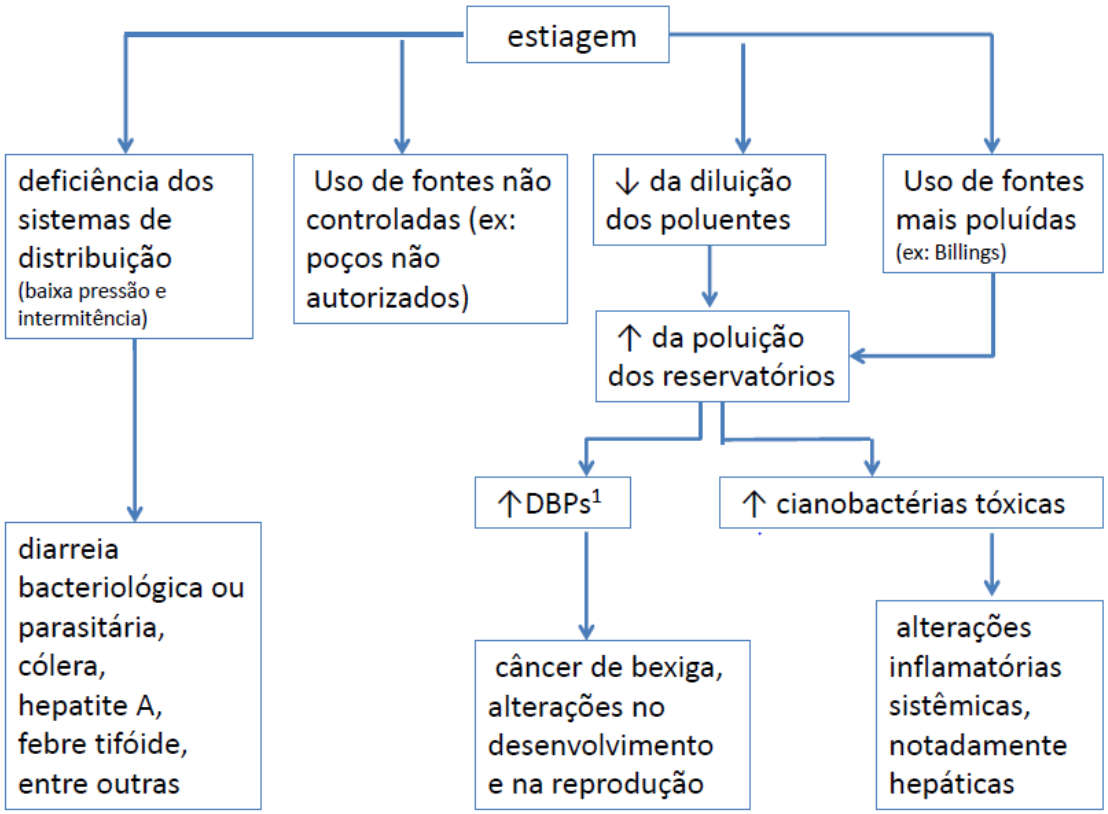
Dentre os variados metabólitos produzidos pelas cianobactérias, muitos são hepatotóxicos, neurotóxicos ou dermatotóxicos (Cheung et al., 2013) e alguns, como a microcistina, são carcinogênicos (IARC 2010) e possuem padrões de qualidade estabelecidos pela Organização Mundial da Saúde. Outras toxinas produzidas por cianobactérias têm graves efeitos de longo prazo, das quais estão a anatoxina (arritmia cardíaca), lyngybia (câncer de pele), cilindrospermopsina (falencia hepática), entre outras (Cheung et al., 2013). A alta concentração de nutrientes na água e o aquecimento global podem favorecer a predominância de toxinas tóxicas sobre não tóxicas (Merel, et al., 2013). A exposição ocorre durante o uso recreativo da água contaminada e pela ingestão direta da mesma.

Em 1988, após um episódio de enchente na Bahia, um surto de infecção gastrointestinal matou 88 pessoas e deixou 2.000 doentes, devido à contaminação por cianobactéria da água para consumo humano da região (Teixeira *et al*., 1993). Em 1996, 52 dentre 116 pacientes de uma clínica de hemodiálise em Caruaru, Pernambuco, morreram devido a presença de microistina na água utilizada na diálise e 89% dos pacientes apresentaram algum sintoma adverso como vômito, náusea, tontura e fraqueza muscular (Azevedo et al., 2002). Além de contaminar diretamente a água através da liberação de toxinas, o aumento das cianobactérias também pode resultar em exposição aumentada aos DBPs (Cheung et al., 2013).

Atualmente, os processos convencionais de tratamento da água, se conduzidos de forma adequada, são efetivos na remoção de toxinas (Cheung et al., 2013). Vale ressaltar que, além de reduzir a incidência de diarreia e outras infecções entéricas, a melhoria na qualidade da água dos reservatórios através do tratamento do esgoto diminuiria os problemas decorrentes do excesso de produtos para tratamento. Uma revisão sistemática concluiu que sistemas de tratamento de esgoto podem reduzir o risco

de diarreia em 30% (Norman et al., 2010), chamando a atenção para a questão da ocupação em áreas de mananciais, origem de parte do esgoto não tratado depositado nas represas. Por diminuir a diluição dos poluentes, a estiagem agrava ainda mais a poluição decorrente do não tratamento do esgoto. A implementação efetiva dos Planos de Segurança da água previstos na portaria federal (MS 2914/2011), (Valentim 2015) seria de grande auxílio no controle sistemático da poluição dos reservatórios.

Figura 1. Possíveis relações entre estiagem, poluição de reservatórios e saúde.



[1] poluição por uso de produtos químicos

2. Alterações do microclima regional

As mudanças do microclima da cidade resultam em inundação de um lado e falta de água do outro, ambos com impactos significativos para a saúde.

Em São Paulo, a diferença de temperatura entre o centro da cidade e a periferia pode atingir até 10ºC. Consequência do processo de urbanização, o fenômeno conhecido como ilha urbana de calor tem origem na substituição da cobertura vegetal do solo por prédios, ruas, avenidas e outras construções de infraestrutura urbana. Tal cobertura do solo absorve mais luz solar, irradia calor e retém menos água, reduzindo a umidade para

evaporação e resfriamento, comparado com a cobertura natural (Sobral, 2005). O desmatamento e a ocupação em áreas de mananciais contribuem para as alterações do microclima paulista. A queima intensiva de combustíveis fósseis por veículos automotores e os altos prédios da cidade que atuam como barreiras para a ventilação, também explicam parte do fenômeno (Sobral, 2005). Como resultado, durante o verão, a diferença de temperatura entre a zona central (quente) e a periférica (menos quente) da cidade aumenta eventos de chuva forte nas partes centrais da cidade (Silva Dias et al., 2013), muitas vezes, sem ocorrência de chuvas nas áreas periféricas, justamente onde se localizam os reservatórios para abastecimento de água das cidades.

Embora desconheçamos estimativas quantitativas da contribuição das ilhas de calor para a estiagem do verão 2013/2014, as alterações climáticas promovidas pelas ilhas de calor têm contribuído para a diminuição da água nos reservatórios ao longo dos últimos anos.

As chuvas fortes favorecem enchentes com efeitos adversos para a saúde humana. Dentre os mais conhecidos e imediatos estão os traumas ortopédicos, afogamentos e doenças de veiculação hídrica como diarreias agudas, febre tifoide, cólera e hepatite A (Du et al., 2010). A água parada da enchente também favorece a reprodução do mosquito aedes aegypti, transmissor da dengue febre e chikunguya e zika vírus. Este último, além de febre, náusea, mialgia e manchas pelo corpo, pode prejudicar o desenvolvimento neurológico dos fetos e recentemente tem sido associado com o aumento significativo da incidência de microcefalia em neonatos no Brasil, mortalidade fetal e síndrome de Guillain-Barré. Segundo dados do site do Centro de Vigilância Epidemiológica do Estado de São Paulo, o número total de casos de dengue no estado de São Paulo saltou de 7.554 em 2013 para 204.236 em 2014, ano de estiagem. Considerando que o verão mais seco reduz o risco de ocorrências de enchentes, o armazenamento residencial de água da chuva para enfrentar o desabastecimento emerge como possível fator colaborador para o surto de dengue. Dependendo da intensidade da chuva e características do local do evento, as inundações podem espalhar diversos químicos industriais e da agricultura, contribuindo para a contaminação da água e floração de bactérias, cujos prejuízos para a saúde já foram discutidos neste artigo.

As ilhas urbanas de calor dificultam a dispersão de poluentes, com prejuízos significativos para a saúde da população no curto e no médio prazo. Além do desconforto geral (ardor nos olhos, alergias, etc.), a exposição de curto período a altos

níveis de poluentes atmosféricos aumenta a incidência de internação hospitalar por doenças cardiovasculares e respiratórias (Braga et al., 2002; Gouveia et al., 2006). A exposição prolongada à poluição do ar aumenta o risco de câncer de pulmão e de morte por causas cardiovasculares e respiratórias (Pope et al., 2002; Fajersztajn et al., 2013). A exposição à poluição do ar ainda está associada com hipertensão gestacional, baixo peso ao nascer e prematuridade (Stieb et al., 2012). O sistema endócrino (Andersen et al., 2012), neurológico (Calderón-Garcidueñas, et al., 2008), entre outros, também são negativamente afetados pela poluição do ar. As ilhas urbanas de calor favorecem a formação de um poluente secundário, o ozônio troposférico, fortemente relacionado a crises agudas de asma (Andrade et al., 2004), alterações cardiovasculares e inflamação sistêmica, além de aumento da mortalidade (Bell et al., 2014).

Ademais, as ilhas urbanas de calor aumentam os períodos prolongados de temperatura muito elevada, conhecidos como ondas de calor e associados com aumento da mortalidade, especialmente por causas respiratórias (Son et al., 2015). No Brasil, o calor extremo foi responsável por um aumento de 7,29% (variação de 7,02 a 7,49%) nas mortes entre 1997 e 2011. A média dos 13 países incluídos no estudo foi de 0,42% (0,39 a 0,44%) (Gasparrini et al., 2015). O aumento da temperatura também impacta a distribuição de vetores causadores de doenças como a dengue (Coelho-Zanotti & Massad, 2012).

3. Considerações finais

A efetividade da gestão da crise hídrica poderá ser alcançada através de um esforço interdisciplinar entre conhecimentos e esferas de governo. A saúde pública pode ser um guia norteador dessas políticas.

Do ponto de vista científico, estudos sobre os impactos da crise da água para a saúde, ajustados para a realidade paulista, ainda são escassos. O momento é uma oportunidade para planejar estudos de longa duração que embasem políticas públicas de gestão da água. Tais estudos podem prever os impactos adversos para a saúde das medidas de gestão da água antes da ocorrência dos mesmos, gerando oportunidades de prevenção. Tais estudos precisam garantir as conquistas da diminuição dos surtos de doenças infecciosas como a diarreia. Ainda, evidências científicas locais robustas sobre os impactos para a saúde individual e coletiva dos químicos emergentes presentes na água podem facilitar a regulamentação desses químicos, medida fundamental para a

proteção da saúde coletiva.

A mídia poderia informar a sociedade de maneira mais efetiva a cerca da dimensão da crise hídrica, combatendo o senso comum de que São Paulo está inserido em uma área de disponibilidade hídrica em quantidade e qualidade suficiente. A segurança hídrica na Região Metropolitana de São Paulo está na pauta dos principais meios de comunicação desde o início de 2014, mas é preciso ir além. É preciso enfatizar outros fatores importantes no entendimento integrado da crise hídrica, que não somente a falta de chuvas. O desmatamento e ocupação em áreas de mananciais, falta de investimentos para a redução de perdas e a má qualidade das águas dos rios por falta de tratamento de esgoto doméstico são exemplos.

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Anexo D.

Registro do protocolo da *overview*[*].Prospero, número de registro CRD 42016043498.

UNIVERSITY of York
Centre for Reviews and Dissemination

NHS
National Institute for Health Research

PROSPERO International prospective register of systematic reviews

Review title and timescale

1 Review title
Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.
Epidemiological time series studies of short-term effects of air pollution: a protocol of an overview of systematic reviews.

2 Original language title
For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3 Anticipated or actual start date
Give the date when the systematic review commenced, or is expected to commence.
26/07/2016

4 Anticipated completion date
Give the date by which the review is expected to be completed.
30/12/2016

5 Stage of review at time of this submission
Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.

The review has not yet started √

Review stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

Review team details

6 Named contact
The named contact acts as the guarantor for the accuracy of the information presented in the register record.
Laís Fajersztajn

7 Named contact email
Enter the electronic mail address of the named contact.
laisfajer@gmail.com

8 Named contact address
Enter the full postal address for the named contact.
Av. Doutor Arnaldo, 455

9 Named contact phone number
Enter the telephone number for the named contact, including international dialing code.
5511988233489

10 Organisational affiliation of the review
Full title of the organisational affiliations for this review, and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Page: 1 / 5

[*] O termo em inglês "*overview*" é usado pelos teóricos em revisão sistemáticas e ainda não possui tradução para o português. Refere-se a revisões de revisões sistemáticas.

Faculdade de Medicina, Universidade de São Paulo

Website address:

11 Review team members and their organisational affiliations
Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

Title	First name	Last name	Affiliation
Miss	Laís	Fajersztajn	Faculdade de Medicina, Universidade de São Paulo
Mr	Samuel	Osório	Faculdade de Saúde Pública, Universidade de São Paulo
Dr	Luiz	Pereira	Programa de Pós-graduação em Saúde Coletiva, Universidade Católica de Santos

12 Funding sources/sponsors
Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.
none

13 Conflicts of interest
List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.
Are there any actual or potential conflicts of interest?
None known

14 Collaborators
Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

Title	First name	Last name	Organisation details

Review methods

15 Review question(s)
State the question(s) to be addressed / review objectives. Please complete a separate box for each question.
Are systematic reviews based on epidemiological evidence from time series studies following major quality recommendation for SRs? - What is the quality of them according to AMSTAR? - Which are the characteristics of the comprehensive search (language restrictions, databases and terms used)? - Which methodologies are being used to evaluate the quality of included studies? - Are they following specific guidelines for SR including SR in environmental epidemiology - Are they registering an a priori protocol? - Are they police recommending polices?

16 Searches
Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.
We will perform a comprehensive literature search of systematic reviews with and without meta-analysis at Pubmed, Embase, Scopus, Web of Science, Cochrane and Lilacs. No language or date restrictions will be imposed to the search.

17 URL to search strategy
If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.

I give permission for this file to be made publicly available
Yes

18 Condition or domain being studied

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.
Daily health events (mortality and/or hospital admissions and/or emergency room visits and/or consultants) due to short-term exposure (up to seven days) to air pollutants.

19 Participants/population
Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.
All populations are eligible for this review

20 Intervention(s), exposure(s)
Give full and clear descriptions of the nature of the interventions or the exposures to be reviewed
Daily air pollution concentrations

21 Comparator(s)/control
Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group).
Not applicable

22 Types of study to be included
Give details of the study designs to be included in the review. If there are no restrictions on the types of study design eligible for inclusion, this should be stated.
Systematic reviews with or without meta-analyses of time-series studies evaluating the short-term health effects of air pollution.

23 Context
Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.
Recently, a growing body of systematic reviews (SR) on the short-term health effects of air pollution are been published, most of them based on evidenced from time-series studies. However, SRs focused on this research question seem not to follow important recommendations for high quality SRs. The previous registration of an a priori research protocol increases transparency and confidence, but apparently few SRs on the short-term health effects of air pollution are registered at specific databases of prospectively registered SRs. Similarly, few SRs on the topic have evaluated the internal validity of the included studies. Difficulties in extrapolating validated quality assessment tools to particularities of time-series studies (e.g. aggregated level data) might explain the scenario. Overviews (reviews of systematic reviews) are useful to evaluate methodological quality and other aspects of these reviews.

24 Primary outcome(s)
Give the most important outcomes.
Daily health events (mortality and/or hospital admissions and/or emergency room visits and/or consultants).

Give information on timing and effect measures, as appropriate.

25 Secondary outcomes
List any additional outcomes that will be addressed. If there are no secondary outcomes enter None.
No restrictions for disease which caused the outcome.

Give information on timing and effect measures, as appropriate.

26 Data extraction (selection and coding)
Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.
Two researchers will independently screen the studies by title and abstract for studies that meet the inclusion criteria. Disagreements will be solved through discussion, after we will retrieve all full reports screened. Two researchers will select studies independently for final inclusion and record the reasons for excluding studies. Disagreements will be solved through discussion. Researchers will not be blind for authors names, institutions or journal titles. For data collection, one reviewer will extract the data and a second reviewer will confirm the information. Disagreements will be solved by discussion. Data extraction will include: - bibliographic details (number and country of authors, journal, impact factor of the journal, search/publication date, language, funding source, number of citations of the review) - search details (databases, period, number of included time-series studies) - major characteristics of the time-series

studies: pollutants, daily outcomes evaluated, population evaluated, subgroups evaluated (age, specific diseases, age group, social economic characteristics, etc.), settlement - Major time-series studies characteristics used to combine studies such as lag between exposure and health event. - methodologies used to appraise the quality of included studies - presence of meta-analysis and its summary effect - other characteristics necessary to evaluate if the SR followed specific guidelines (Mose, Prisma and Blair et al., 1995, Navigation Guide and/or National Institutes of Environmental Health Sciences National Toxicology Program). - other characteristics necessary to evaluate if the SR made police recomendations

27 Risk of bias (quality) assessment
State whether and how risk of bias will be assessed, how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.
Two researchers will independently appraise the methodological quality of the systematic reviews using the Measurement Tool to Assess Systematic Reviews (AMSTAR) tool. Disagreements will be solved through discussion. To the extent that Amstar work with scores, we will also evaluate the information extracted qualitatively.

28 Strategy for data synthesis
Give the planned general approach to be used, for example whether the data to be used will be aggregate or at the level of individual participants, and whether a quantitative or narrative (descriptive) synthesis is planned. Where appropriate a brief outline of analytic approach should be given.
We will perform a descriptive synthesis of the data.

29 Analysis of subgroups or subsets
Give any planned exploration of subgroups or subsets within the review. 'None planned' is a valid response if no subgroup analyses are planned.
None planned.

Review general information

30 Type and method of review
Select the type of review and the review method from the drop down list.
Epidemiologic, Systematic review

Public health (including social determinants of health)

31 Language
Select the language(s) in which the review is being written and will be made available, from the drop down list. Use the control key to select more than one language.
English

Will a summary/abstract be made available in English?
Yes

32 Country
Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved. Use the control key to select more than one country.
Brazil

33 Other registration details
Give the name of any organisation where the systematic review title or protocol is registered together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here.

34 Reference and/or URL for published protocol
Give the citation for the published protocol, if there is one.
Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with CRD in pdf format.

I give permission for this file to be made publicly available
Yes

35 Dissemination plans
Give brief details of plans for communicating essential messages from the review to the appropriate audiences.
Do you intend to publish the review on completion?
Yes

36 Keywords
Give words or phrases that best describe the review. (One word per box, create a new box for each term)
Epidemiologycal time series studies

systematic review and meta-analysis

quality assessment

police recommendation,

air pollution

health

environmental epidemiology

37 Details of any existing review of the same topic by the same authors
Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.
Not aplicable

38 Current review status
Review status should be updated when the review is completed and when it is published.
Ongoing

39 Any additional information
Provide any further information the review team consider relevant to the registration of the review.

40 Details of final report/publication(s)
This field should be left empty until details of the completed review are available.
Give the full citation for the final report or publication of the systematic review.
Give the URL where available.

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