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Exposome Research in the Perspective of *longue durée* Political Epistemology

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Introduction

The exposome has developed over the last two decades as an integrative approach to the study of the effects of the environment on human health. This new field has already been the object of intense scrutiny from the social sciences, interrogating its historical novelty, epistemological foundations, and policy consequences. Exposomics has often been interpreted in postgenomic terms – that is, in the context of the approaches developed after the Human Genome Project, with the goal of extending or updating its results and, more specifically, reacting to the limitations of gene-centric approaches. This contribution aims at (i) developing a synthesis of this scholarship and (ii) broadening the contextualisation of exposomics. We do so by adopting the complementary lenses of a *longue durée* historical perspective to discuss the *political epistemology* of exposomics. A longer-term historical perspective is mobilised to identify recurring features pertaining to how societies dealt with the role of the environment on human health: the interlinking of a *theoretical perspective* and a *sociocultural context* that result in *modes of translating this knowledge into practical recommendations*. Explicit attention to the political epistemology of exposomics, in turn, clarifies the various ways in which exposomics is situated, thereby enabling its normative assessment. In turn, this analysis of the exposome aims to illustrate the fruitfulness of an *integrated* historical and philosophical perspective, as both approaches complement each other to contextualise exposomics, and outline pathways of future developments. We consider that this broader perspective is also helpful to illuminate, beyond the exposome, the recurrent features and trade-offs faced by other (and probably future) approaches to study the role of the environment on health.

Building on this context, we add a novel contribution to current debates on the exposome. Instead of characterising how the exposome – in a postgenomic context – marks a renewed focus on the role of the environment, we show how it is a contemporary *instantiation* of a secular attempt to shape (and improve) body/environment configurations and we sketch analytic tools to provide a descriptive and normative assessment of such approaches. This double aim weaves together insights from an interdisciplinary corpus comprising contributions from history, philosophy, and social studies of science, along with reflexive analyses from practising scientists. *Section 1* introduces the readers to the exposome: its conceptual and methodological basis, and practical ambitions. *Section 2* expands the historical narrative in which exposomics has been traditionally inserted, replacing the 'postgenomic' moment with a *longue durée* perspective, moving interpretations of the exposome beyond the view that it is merely a holistic response to previous gene-centric reductionism. *Section 3* applies the framework drawn from this historical analysis to synthesise criticisms subjected to exposomics, and jointly considers epistemological and political dimensions. This integrated historical and philosophical analysis allows us, in *Section 4*, to reflect on possible paths of development for exposomics, providing considerations that are hopefully relevant to future scientific endeavours lying at the intersection between the environment and human health.

1. *Welcome to the exposome*

The exposome has initially emerged as a conceptual proposal, from molecular epidemiologist Christopher Wild, to designate the *totality of environmental exposures experienced by an individual at any given point in life, from their conception onwards* (Wild, 2005, p. 1848). This ambitious (and encompassing) stance emerged in the aftermath of the *Human Genome Project* (HGP). The completion of the sequencing of a full genome of human DNA was expected to clarify the genetic basis of human traits and heritability, thereby providing scientists and society with a vastly improved understanding of the aetiology of diseases as well as targets for therapeutic interventions. These expectations have not been met, and have instead pointed to the major role played by *environmental* factors. The notion of the 'exposome', in this context, is meant as a provocative invitation to invest similar scientific and economic means, and draw equivalent public attention, towards a better characterisation of the environment than it has been invested in deciphering the genome.

The exposome has since developed into a novel approach to studying the role of the environment in human health. It has gained institutional currency through journals, courses, inscriptions on legal texts, and above everything large-scale scientific projects. In 2020, and after funding individual projects, such as *EXPOsOMICS*, *HELIX* and *LIFEPATH*, the European Commission has recently dedicated more than 100 million euros to the *European Human Exposome Network* (EHEN), where 9 projects involve 126 research teams across the continent (Fayet et al., 2024).

These large-scale projects involve a multidisciplinary assemblage of epidemiologists, toxicologists, bioinformaticians, data scientists, legal scholars with the aim of overcoming the respective limitations of these individual perspectives. It particularly aims to bring together, on one side, the insights and analytic precision brought by laboratory sciences with, on the other, the advantages of large populations and long time-scales afforded by cohort studies. Doing so, it harnesses the opportunities brought by recent developments in big-data sciences to increase the volume, velocity and variety of data created and analysed. Exposome projects are characterised by their dedication *not* to focus on any singular exposure in particular, but rather to an exploration of the conjoined simultaneous and long-term effect of exposures on health. Concretely, this involves crossing 'omics' data, high-throughput analyses of a given substance from a biological sample, with a variety of data tracking external exposures collected through sensors, geographic information systems, wearable devices, administrative registers and questionnaires.

Optimistic characterisations of exposomics have highlighted its potential to unravel the aetiological 'black box' traditionally associated with epidemiological research. Epidemiology has been, in this view, historically marred by the difficulty of identifying causal relations from correlations between exposures and health outcomes. Exposomics, by providing an extended characterisation of the individual, physiological effects of external exposures (including social ones), promises to illuminate how the environment 'gets under the skin' and

affects biological processes (Ghiara & Russo, 2019). Such improved knowledge, in turn, is seen as providing better grounds for the formulation of health-promoting policies, for instance through the identification of early risk factors on which to focus political attention. In other words, the hope behind exposomics is that «[p]ublic health strategies could finally lean on the biomedical knowledge that it has historically lacked» (Arminjon, 2023, p. 66). Exposome projects, in this aim, integrate within their team policy, legal, and ethics experts. They also increasingly include elements related to participatory science, which would enable stakeholder involvement at the level of knowledge constitution and policy formulations. In a similar vein, increased attention – in the more recent projects – is placed on devising scores and indicators that could translate (potential) external exposures into assessments of individual and population-level risks and evaluate policy proposals through cost-benefit analyses (Fayet et al., 2024).

In sum, exposomics presents itself as an integrative approach to the role of the environment on human health and disease, combining «breadth of scope and precision, scientific excellence and policy relevance» (Fayet *et al.*, 2024, p. 2). This idealistic narration has been criticised on both historical and epistemological grounds. We propose, in the next two sections, to extend these criticisms by successively broadening their historical (*Section 2*) and epistemological (*Section 3*) focus.

2. *Towards a longue durée view of exposomics*

2.a. *Exposomics as postgenomic science*

Existing analyses have, to a certain extent, embraced the historical narrative proposed by advocates of exposomics, where the exposome is an idea born and motivated from the disappointments of the HGP. This explicitly frames exposomics as a *post*genomic project and its possible novelties thereby need to be assessed in the light of the preceding focus and hopes garnered around genetic sequences. In this view, the development of exposomics comes at a time of shifts, where «[o]nce marginal critiques of a gene-centric vision of the life sciences are now moving to the center of the action» as scientists brace to find «the key to human health […] in the delicate networks of gene regulation in their biochemical, cellular, and ecological environments» (Richardson & Stevens, 2015, p. 234). This historical framing matters, according to Richardson & Stevens, not only to document these recent transformations. It is also «crucial in understanding not just how biology will develop but also where the sciences (and perhaps also the social sciences) are headed in the coming decades» (Richardson & Stevens, 2015, p. 240).

The postgenomic framing, on one hand, highlights the adoption by scientists of a more holistic point of view, and the increased attention to environmental and developmental factors. This opened up the possibility of new ways for social scientists to engage with the natural sciences (Shostak & Moinester, 2015, p. 239). Interdisciplinary collaborations would here be celebrated as an

antidote to the partiality and lack of reflexivity characteristic of one-sided genetic projects. In a similar vein, postgenomic science is seen as being increasingly explicitly geared towards public and policy engagement, crafting scientists as «public reformers, stewards of justice», embracing strategies of local empowerment and «bringing a social equality framework into the heart of research» (Bliss, 2015, pp. 185-186). This encompassing approach, according to Bliss, «permits postgenomic scientists to make their research goals take priority over health disparities that take a more sociological approach» (Bliss, 2015, p. 186).

Conversely, viewing exposomics as an instance of postgenomic sciences underlines its continuities with genomics, portraying it partly as an expansion of its core methodological commitments and its overall ambitions. As Shostak & Moinester point out, postgenomics' explicit will to be politically relevant is also typical of genomics's tendency «to promise big» (Shostak & Moinester, 2015, p. 239). In this view, exposomics is presented as expos-*omics*, the «characterization at the 'omic' scale of non-genetic drivers of health and disease» (Giroux, 2021, p. 14, our translation). Exposomics would, in other words, result from the expansion of the genome sequencing technologies, which provide «a shared platform for biological research across many fields and social arenas» (Stevens & Richardson, 2015, p. 3) and an ethos of «large databases, multidisciplinary teams, data sharing, high-throughput data collection and experimentation, hypothesis-free discovery, and massive computation» to new layers of the biological and social reality (Shostak & Moinester, 2015, p. 240). In similar terms, Canali presents the exposome as an extension of the «sequencing repertoire […] from a material and methodological perspective, leading to the conceptualization of an environmental equivalent to the genome and the broadening of the concept of exposure to make use of omics data» (Canali, 2020, pp. 2-3). In doing so, the exposome is similar to other disciplines and approaches, «as diverse as neuroscience, ecology, music, economics, political science, and sociology», that «adopt aspects of the genomic approach» (Shostak & Moinester, 2015, p. 240).

Alternate contextualisations have depicted exposomics as the conjunction and meeting point of broader developments within population health sciences. In addition to postgenomics, Canali highlights how exposomics borrowed from exposure sciences key «conceptual and methodological tools to look at internal exposure as a type of exposure», from molecular epidemiology its emphasis on the precise characterisation of exposure at the molecular level, and from sociology its insistence on a life-course perspective, looking for the long reach of (early) life events into health outcomes (Canali, 2020a; see also Giroux, Fayet, Serviant-Fine, 2021). The novelty of exposomics resides, here, in the «new contextualization, repurposing and significant variation» resulting from integrating these fields within epidemiology (Canali, 2020a, p. 3). This offers «a window», then, «through which epistemological changes for both biomedical and environmental research can be analysed» (Canali & Leonelli, 2022, p. 206).

2.b. *Adopting a Longer-Term View: Exposomics as Contemporary Neo-Hippocratism*

The postgenomic contextualisation of the exposome is an attempt to highlight and explain the *novelties* borne with exposomics. Yet this framing locates these novelties in the confines of a relatively short temporal horizon and tends to view and evaluate it primarily as a response to the reductionism of its direct predecessor. It remains, at the farthest, within the scope of 20th-century science, while focusing mostly on the developments at the century's tail end. *What do we learn of the exposome, instead, if we adopt a longer-term view?* In this subsection, we describe the exposome not as the pinnacle of contemporary population health research, but as an instantiation of a secular practice that aims to understand the effects of the environment on human health and, from this knowledge, act to improve it. This mutual influence between knowledge practices and political priorities is what we designate as a *political epistemology*.

Discussing the contemporary popularity of the term «personalised medicine», Guchet wonders how «a term that trivially summarises the whole past of medicine, and has even always seemed to define it, nowadays serves as a programme for its future» (2019, p. 73, our translation). While the concept of exposomics is undeniably a recent invention, similar remarks could be made about its purview, namely, a holistic understanding of how environments impact human bodies. While its novelty is clear when compared to the pronounced gene centrism of the 20th century (Fox Keller, 2000), a broader dive into historical scholarship presents it instead as a secular practice – inscribing it in the *long legacy of Hippocratism*.

Hippocratism, a set of doctrines attributed to Greek physician Hippocrates (around 400 BC), emphasises the influence of environmental factors – the 'airs, waters and places' triad – on the body's 'humoral balance', a set of vital body fluids determining the health status of individuals. Hippocratic physicians developed a rather holistic attentiveness to «the seasons, the waters, the prevailing winds, and the physical geography and soil of a place», all factors presumed capable of bearing health impacts (Bashford & Tracy, 2012, p. 496). The influence of this view, however, goes beyond medical practice as we understand it. Archaeological research tracks the concrete traces of Hippocratism on the localisation, design of built environments, and military strategies. It regimented the function and behaviour adopted in public institutions such as public baths and thermae (Meloni, 2021, pp. 338-339).

The legacy of Hippocratism is to be seen as a tradition of framing the relation between human bodies and their environments that has «proved remarkably resilient and adaptable, redeployed in diverse historical contexts across time» (Bashford & Tracy, 2012, p. 497). Historians, here, argue against the idea of a discovery, or rediscovery, of this attentiveness to the role of the environment on health, for «it was never entirely forgotten» (Rosenberg, 2012, p. 666) but rather replayed, even in contemporary contexts, through new tools and new languages (Rosenberg, 2012, p. 670). In other words, «our present anxiety to govern biological plasticity is neither unprecedented nor the result of a linear unfolding of scientific growth» (Meloni, 2021, p. 335) but the reenacting of our

understanding of the «precariousness of the body/environments boundary» (Meloni, 2023, p. 3).

This permeability of the body with its environment, which both «sustains and threatens it» (Rosenberg, 2012, p. 668) as a «deeply beneficial and a dangerous intruder» (Meloni, 2021, p. 338) is a noted continuity from Hippocratism to today. It results in an understanding, still relevant today, of population patterns of health and disease, morbidity and mortality, as shaped by the characteristics of their environments. Another thread that carried over to contemporary thinking is the vision of disease as emerging from a multicausal, cumulative process, something that can be thought «as an aggregate insult» (Rosenberg, 2012, p. 668). Practising Hippocratic medicine requires, in addition, what we would nowadays call interdisciplinary knowledge (or, similarly, would require the conjoined expertise of experts from several disciplines). It depicts «a clinician who is an obligate climatologist, geographer, political scientist, and ethnographer as well as a healer» (Rosenberg, 2012, p. 661).

Despite these «striking if schematic continuities» (Rosenberg, 2012, p. 668), contemporary attention to the role of environments on human health bears important specificities. A legacy of our increased understanding as globally situated, humans are not anymore seen as dependent but *interdependent* with the environment. The Hippocratic worldview did not conceive «the cumulative impact of humankind on the natural world» (Rosenberg, 2012, p. 669). We have developed a vision where human interventions and ideas have had both environmental and biological consequences, creating «socially modulated biologies» (Landecker & Panofsky, 2013, p. 351), which can lead to attempts to «heal the body in the world that humans have made for themselves» (Landecker, 2011, p. 190). As a consequence, contemporary researchers investigate factors that are shaped by humans, and came to situate «the body in time as well as space» (Rosenberg, 2012, p. 668), within intra-individual and intergenerational trajectories.

Inserting exposomics within the legacy of Hippocratism rather than postgenomics highlights its deeper historical continuities and reinterpretations. As we illustrate in the next paragraphs, it shares with its forerunners an articulation of what Krieger conceived as «key features of any epidemiologic theory», that is, an «*interrelated sets of ideas – including both substantive and explanatory concepts – for describing, explaining, and ultimately transforming population distributions of health, disease, and well-being*» (Krieger, 2024, p. 32). In other words, theories set causal and investigative priorities, and thereby define a space of possibilities for action and intervention (Krieger, 2001; Canali & Leonelli, 2022). The understanding of bodies as open and porous with their environments has opened a window for environmental intervention, and, as illustrated below, constitutively links it to social and political questions (Müller et al., 2017). Together these examples map responses to «the problem of how to live with a porous body at the individual and collective level» (Meloni, 2021, p. 342).

2.c. *Neo-Hippocratism in Practice*

Pre-modern attempts to collectively regulate the environment, as recently reviewed by Meloni, deal with efforts to keep airs and waters clean, as well as the quality of the sold merchandise. They were not only enforced through policing by the power institutions in place (through specially appointed public officials, fines, court orders), but also by a proactive engagement of citizens and local elites (Meloni, 2021, pp. 340-341). This vision was «shaped by medical knowledge, and operationalized through the establishment of a legislative corpus for health and environmental regulation, town doctors, and in some cases, boards of medical experts» (Meloni, 2021, p. 339).

In the medieval period of urban expansion, between the 11th-13th century, works such as those of Ibn Sina (also known as 'Avicenna') constituted both the main medical influence of its time and a synthesis from «Persian, Arabic, Greek and Indian sources» (Meloni, 2021, pp. 339-340). This knowledge informed modes of policing and surveilling the public space (through registers and record-keeping), notably to quickly respond to possible epidemics. Similarly, a study of medieval Valencia, in the 1300-1500 period (Agresta, 2016), shows how the town's environmental policies «reflected perfectly a humoralist understanding of free flows and evacuations to expel the excess of plethora and humoral imbalance», thereby displaying how religious and medical beliefs were entangled in the shaping of interventions «for the *salut* of the civic body» (Meloni, 2021, p. 341).

Another example of the socio-political use of theories on the role of the environment to shape human health is found in the Modern period of European colonial expansion, described as a «grafting of climate, race, and physiological determinism» (Bashford & Tracy, 2012, p. 498). The permeability of the body to climate influence here builds on essentialist assumptions about racial hierarchies and distinctness, and the joint task to adjust the bodies of colonisers to the «dangers and peculiarities of their local environments» (Rosenberg, 2012, p. 664) as well as to «control the health of the local labouring populations» (Meloni, 2021, p. 339). In all such circumstances, responses of the colonisers and the colonised to (interventions on the) climates, atmosphere, food, and fauna were carefully recorded and investigated.

The efforts of public health reformers, in the 19th-century United Kingdom and the United States, were instead inscribed in the context of the Industrial Revolution and the growing realisation of the nefarious effects of cities on the health of its inhabitants. The background assumption, here, is that «local environments provided both explanation and solution for the shocking differentials in mortality and morbidity that marked country from city, townhouse from tenement, the holds of ships or crowded military camps from farm or village» (Rosenberg, 2012, pp. 662-663, our emphasis). As symbolised by Rudolf Virchow's slogan, «*Medicine is a social science, and politics nothing but medicine at a larger scale*», proponents of Social Medicine explicitly tied the management of *socially-produced* environments to matters of governance. In this view, «climate and local circumstances stood at the center of aetiological thought», and the dispropor-

tionate burden of illness borne by the poor and the socially deprived was at the center of the agenda for explanations and interventions (Rosenberg, 2012, pp. 663-664; Bashford & Tracy, 2012, p. 503).

This attentiveness to the differential and detrimental effects of environments on health is also shared by reformist intellectuals from 20th-century interwar United States, who «sought to reform the political organization of the United States and defend a system of social protection» (Arminjon, 2023, p. 70; see also Timmermann, 2025). Among those «scientist-activists», Cannon is credited as being «one of the first, if not the first, to biologize and molecularize stress» (Arminjon, 2023, p. 69). His notion of 'homeostasis', which designates the ability of the body to maintain its physiological equilibrium, is to be understood as providing a biological basis to the body's reactions to its environment. Investigating the biological level, here, is meant to complement, and not compete, with a thorough documentation of the social level. On the contrary, it is meant to provide further objective knowledge to document, and thus legitimate interventions on structural causes of social inequalities in health, in order to both prevent them and alleviate their effects (Arminjon, 2023, p. 71). These reformist intellectuals mark another instance of the inherent intricacy of conceptual, epistemological and political dimensions at the intersection of environment and human health.

These interests in the biological effects of social environments fed the development, in the second half of the 20th century, of the discipline of *social epidemiology*. Its practitioners «made plain that the environment was socially and politically mediated, […] and [focused] explicitly and prescriptively on the social inequalities that shaped human health», reiterating an engagement that is inseparably scientific and political (Bashford & Tracy, 2012, p. 505). Its discourse simultaneously speaks «of society and biology», and seeks to describe «how we literally incorporate, biologically, the world around us» (Krieger, 2001, p. 668). The task of theory, here, is to draw attention, in specific contexts, to the «societal and biological processes involving phenomena within and across levels within and over different scales of time and space» (Krieger, 2024, p. 247). This involves deciphering the interaction of «societal arrangements of power and property and contingent patterns of production, consumption, and reproduction» with «constraints and possibilities of our biology» (Krieger, 2001, p. 672). This tall order is, in the view of social epidemiologists, an inevitable one to avoid the pitfalls of both «incomplete understanding and potentially harmful consequences» (Krieger, 2024, p. 311), and forces to rethink our understanding of the aetiology of (and thereby interventions to address) population differences in, for instance, blood pressure, diabetes or disease susceptibility such as peptic ulcers.

Our catalogue of historical examples closes with what appears to be the epitome of an *antithesis* to the attention of the environment on human health. In the uninhibited gene centrism of its most vocal promoters, the HGP appears in fact as proposing a clear (if simplistic) project that articulates scientific knowledge and policy interventions. Its legitimacy is premised on the claimed

futility of investigating environmental factors, as genes and genomes dictate our fate, and is therefore the site in which to search for solutions to address «the horrors of the deranged mind» (Panofsky, 2015, p. 154, citing James Watson, first director of the HGP). This vision reduces interventions of the social factors to «'Band-Aid' solutions that fail to address the real, genetic roots of the problem» (Panofsky, 2015, p. 154, citing Daniel Koshland, who worked at the time as editor of *Science*). The negation of the fundamental importance of the environment on health, as championed by the HGP, is therefore in itself a «road map for geneticists to insert themselves at the center of crucial public issues» (Panofsky, 2015, p. 154).

2.d. *Back To the Exposome*

The aim of this succinct historical detour through the long legacy of Hippocratism is neither to pave a teleological narrative culminating in exposomics, nor to adjudicate, through ahistorical norms, the merits of these different approaches. It is, instead, to display how the project of understanding the role of the environment on health (or, as with the HGP, to explicitly negate its importance), always already involves the conjunction of theoretical views of the aetiology of health and disease and of socio-political priorities. Together, they influence the way the environment is investigated and intervened upon. While the framing of the exposome as a postgenomic science is useful to emphasise the novelties and renewed opportunities that this approach provides in relation to its gene-centric precedent, we have shown that it is also a contemporary instantiation of a secular articulation between knowledge and intervention. This shows the broader *situatedness* of the exposome. It encourages us to clarify the *joint* articulation in exposomics of an aetiological view; an epistemological structure; and a way to translate this knowledge into health-promoting interventions. In doing so, this historical analysis of exposomics draws attention towards its *political epistemology*. We argue in the next section that this integrated historical and philosophical perspective deepens our descriptive and normative understanding of exposomics.

3. *Towards a Political Epistemology of Exposomics*

The *longue durée* historical analysis of the previous section provides significant results and a starting point for our next step. It shows that exposomics is part of a long history of relations between the environment and health and of different uses of medical knowledge to monitor, investigate, and act upon the environment. More specifically, this historical narrative indicates how theoretical and epistemic choices, on the one hand, and socio-political priorities and real-world consequences, on the other, have continually shaped each other. In this section, we show how this mutual shaping operates in the case of exposomics, by examining its political epistemology, which we take to mean the interlinkage between its theoretical frameworks, its epistemic priorities, and its space of policy interventions on the environment, with implications that are political as

much as epistemological (Omodeo, 2019; Frickel and Moore, 2025). More specifically, we discuss the two main theoretical frameworks that have emerged in exposomics so far and show that these (although they might seem mostly technical choices about how to partition exposures) have significant and interrelated epistemological and political implications. These approaches provide heuristics – for instance, for producing evidence – but in this sense also limit which interventions can be evidence-based and feasible.

3.a. *Internalist and Integrative Exposomics*

At stake in developing a clear theoretical framework for exposomics has been to avoid falling for an «undifferentiated 'holism'» (Krieger, 2024, p. 247). The risk is compounded by the variety of things, in our contemporary lexicon, that can denote the 'environment'. This includes «the cell (the environment of the gene), endogenous hormonal profiles (the environment of the cells), indoor or outdoor ambient environments (the environment of the human body), social networks, poverty, and/or stressful life situations (the social environment)» and even «individual behaviors, such as diet and exercise» (Shostak & Moinester, 2015, p. 194). All of these elements, in principle, are part of the conceptual scope of the exposome.

Exposomics researchers, in this context, have fluctuated through various definitions (Giroux, 2021), with the emergence of a partition between *internal* exposures, the bodily processes (metabolism, the endocrine system, the immune system…) that surround cells and tissues, and *external* exposures of a tangible kind (a given agent or substance in the environment) or a less tangible one (related to psychosocial and economic influences) (Wild, 2012, p. 24). Among these dimensions, analyses of exposome projects describe a general tilt towards internal exposures, with the external exposures that are considered mostly insofar as they can be correlated with outcomes observed at the internal level (Merlin & Giroux, 2024). We designate this orientation as *internalist* exposomics, which aligns with the search for causal explanations that would account for how «socioeconomic factors 'get under the skin' and affect the biological level […]» (Ghiara & Russo, 2019, p. 10). It aims to develop a «biological index of our nurture» in the sense of retracing «the cumulative measure of environmental influences and associated biological responses throughout the lifespan» (Miller & Jones, 2014, p. 2). At the same time, there is another theoretical framework that we call *integrative* exposomics. This has been suggested by other proponents of the exposome (Wild, 2005; Giroux, 2023) and is increasingly presented as a possibility to overcome initial limitations of exposome projects.

As we show next, these two possible interpretations have downstream epistemic and political consequences for exposomics: the first, *internalist* exposomics, maintains the field's current tilt towards internal exposures; the second, *integrative* exposomics, assesses the field as it moves forward.

3.b. *Epistemic Consequences of Internalist and Integrative Exposomics*

In the internalist version of exposomics, where research primarily targets internal responses to a multifaceted environment, methodological priorities are set accordingly. It provides researchers a heuristic, a «regime of perceptibility» (Shostak & Moinester, 2015) that «proceeds from the internal effects of exposures to relevant external exposures» (Merlin & Giroux, 2024, p. 13). This lends to a recurrent critique levelled at exposomics: the selective attention towards what satisfies this common denominator, that is, the consideration of external factors insofar as they can be associated to consequences measurable at the internal, individual level. Doing so, exposomics risks rendering invisible factors that cannot be thereby detected, in particular socio-political factors that play out at the collective level. In other words, «exposomics might have the unintended consequence of recasting even the most socially determined exposures as individual traits» (Shostak & Moinester, 2015, p. 203).

By contrast, achieving an integrative exposomics which blends «multiple levels of analysis and techniques of measurement» (Shostak & Moinester, 2015, p. 205) requires overcoming a series of epistemological obstacles. The first is at the level of data *interoperability*. How to define a common metric, a way to fruitfully combine, compare and associate measurements from all of the corners of the exposures? This challenge is compounded by the one of data *quality*. Exposomics combines the results from new and extant longitudinal studies, collected in different sites with possible technical differences and access to data. A successful multidimensional analysis relies on data that are both sufficiently homogenous and sufficiently abundant for a given exposure. Researchers of the LIFEPATH project, for instance, highlight the paucity of cohorts that satisfy the demand for combining «a good measure of socioeconomic status, of risk factors of noncommunicable diseases and of already measured biomarkers» (Vineis et al., 2017, p. 422). Thirdly, it is important to be aware of the myriad of assumptions (which could be epistemic or non-epistemic) that drive the constitution and association of the different exposures analysed (as documented by Canali, 2020b for EXPOsOMICS). All these steps can be seen as establishing the «evidential and representational content» of a dataset, in order to legitimise the inferences derived from the integrated datasets as «a representation of specific relations between exposure and disease» (Canali, 2020b, p. 6). Put together, an integrative exposomics requires the overcoming of methodological challenges helped by an awareness of the assumptions and choices that permeates the constitution of its data.

3.c. *Political Implications of Internalist and Integrative Exposomics*

Because epistemic choices structure what counts as evidence, they also delimit which interventions appear feasible, constraining its political implications. These differ markedly depending on whether assessing exposomics in its internalist or integrative orientation. While the former is the most routinely criti-

cised, it matters to ask to which extent the political scope of exposomics changes in its integrative version.

An internalist orientation is considered to be particularly amenable to the development of interventions at the individual level or for individual exposures. This includes behavioural recommendations, prevention strategies centralised on a given exposure, or the development of clinical or therapeutic interventions. In this mode, internalist exposomics emulates the model from the biomedical sciences, also conceived as «evidence-based practice», which harnesses statistical analyses of correlations between quantifiable parameters, and is used to «devise specific, targeted, and cost-effective public health actions» (Serviant-Fine et al., 2023, p. 6). This vision is broadly criticised for reducing public health action to technical problem-solving. Doing so is achieved at the detriment of an engagement with the socio-political conditions that underline the (differential) exposures to health-promoting or pathogenic factors (Guchet, 2022; Giroux, Fayet, Serviant-Fine, 2021; Serviant-Fine *et al.*, 2023; Shostak & Moinester, 2015). Moreover, the «uptake of biomedical standards of evidence may overshadow intrinsic methods of proof-making in social science» (Serviant-Fine *et al.*, 2023, p. 6) and thereby dispense with potentially valuable sources of knowledge.

An assessment of the political consequences of integrative exposomics has been recently proposed through a critical analysis of the profile papers of the European Human Exposome Network (EHEN), which detailed their ambitions, priorities, and methodological choices (Fayet et al., 2024). It revealed an intensification on all fronts, from the volume and variety of data, the infrastructure for data analysis, the production of operationalisable knowledge and the breadth of scope of addressed public health priorities. Underlying all of this, however, this analysis made visible the *socio-spatially* situated character of this new wave of projects: exposomics is mostly geared towards *wealthy urban contexts*. It does so through its data intensiveness that requires a well-developed data infrastructure, through explicit focus towards urban health (i.e. the EXPANSE project) and implicit biases from measures (i.e. air pollution, noise, and built environments) and indexes (i.e. walkability scores, accessibility to food outlets or green spaces) that are mainly (if not solely) relevant to such environments. While providing knowledge to «help the design of healthier urban environments», such research «risks widening other spatial inequalities at regional, national and European scales since affluent urban areas are already benefitting from the best overall health outcomes in many European countries» (Fayet et al., 2024, p. 6).

Both internalist and integrative versions of exposomics, though distinct, thus face significant limitations in their political scope. The former through a technicisation of public health issues that downplays structural determinants, the latter through a socio-spatial bias that caters mostly for wealthy (and healthier) urban environments, thereby possibly furthering spatial inequalities of health.

By considering the restricted value of exposomics – whether internalist or integrative – to address public health priorities, in particular by questioning its overall effect on social inequalities in health, both lines of criticism question the need to resort to scientific projects of such scale and complexity. More precisely, exposomics' conceptual holism, explanatory ambition and, thereby, hegemonic stance leads to an underestimation of the knowledge already present, and perhaps already sufficient, to address public health priorities. As previously mentioned, embracing an evidence-based approach to devising and legitimising public health interventions is suspected of hiding the «full extent of social and epidemiological knowledge *already available* for transformative public health action» (Serviant-Fine et al., 2023, p. 7). Moreover, its methodological sophistication, restricted vision of causality and difficulty to implement in practice might lead to entrenched methodological debates that lose sight of the possibly limited relevance of such approaches (Krieger, 2001; Valles, 2021; Kelly-Irving et al., 2022). Not only can these epistemic standards prove inadequate, but the difficulty to satisfy them can, moreover, provide «epistemic justification for political inaction» (Fayet et al., 2024, p. 6).

4. *Mapping the Possible Futures of Exposomics*

Reconstituting the political epistemologies of exposomics thus tracks how theoretical and epistemic choices on one side and socio-political priorities and real-world consequences on the other mutually shape each other. Taking stock of our analysis, this last section translates the longue durée analysis of exposomics into normative evaluations of its possible futures.

There is a specific if implicit assumption behind both of the previously outlined theoretical frameworks of exposomics: increasingly complex and exhaustive knowledge will inspire increasingly precise and efficient policy interventions. Complex scientific knowledge is here presented as a prerequisite for political relevance. This is for instance a core aspect of the Russo-Williamson thesis (for a similar view on obesity science, see O'Malley & Stotz, 2011), that proposes that «the better our understanding of the disease and its development, the better our actions to reduce its burden on the population» (Russo, 2012, p. 142). The emphasis on deciphering «mixed biosocial mechanisms» – causal explanations of the trajectory from environmental exposure, understood broadly, to disease outcomes (Ghiara & Russo, 2019; Rod et al., 2023) – is compatible with either internalist or integrative visions.

However this assumption needs to be reconsidered, in light of the results of our analysis in the previous section: does exposomics actually provide *evidence for use* in a *well-ordered* science of the interactions between the environment and health? We take these terms from Cartwright, who, following Kitcher (2001), asks whether scientific investigations are geared towards the *right* questions and, if so, whether scientific methods «can get us the kinds of results we are really looking for» (Cartwright, 2006, p. 982; see also Valles, 2019). Beyond the goal of developing increasingly complex and exhaustive knowledge for more

precise and efficient policy interventions, there seems to be a mismatch between holistic and conceptual intentions – the idea of capturing the health effect of the whole of biological and social exposures – and how exposomics is performed in practice and translated into policy decisions.

Even in its most ambitious – integrative – version, exposomics still ends up «highly situated – rather than holistic and inclusive» (Fayet et al., 2024, p. 7). We concur, thereby, that the limits of exposomics' possible «contribution to public and environmental health needs to be explicitly recognized» (Fayet et al., 2024, p. 7). This similarly requires an increased awareness of its conceptual basis, of the variety of assumptions that drives its methodologies, and of how these delineate epistemological and political limitations. In the absence of awareness of its situatedness, the mere search for more complex knowledge by chasing more data and crunching them with more developed analytic infrastructure will not mechanically turn into better policy interventions. In doing so, our project aligns with recent philosophical approaches foregrounding the crucial importance to recognise the pervasive influence of values in scientific research (Elliott, 2017) and to focus on a practice's «intrinsic ethics» (Tuana, 2010, 2012).

This combination of a *longue durée* historical perspective with an explicit focus on political epistemology, and a more explicit engagement with the situatedness of a scientific approach, is important not only to understand and assess projects such as exposomics, but also brings this approach in contact with historical precedents and contemporary projects at the intersection of human health and the environment, thereby *helping to outline possible futures*.

It is important, for instance, to be reminded that the deciphering of the physiological impact of social factors does not necessarily lead to an «individualization and desocialization of health problems» (Serviant-Fine et al., 2023, p. 14). Historically, this research – in the legacy of Cannon's work on homeostasis – has instead been mobilised to provide «a gain of objectivity that plainly participates in the struggle against social inequalities in health» (Arminjon, 2023, p. 67) by giving further political traction to the necessity to fight its social and political causes. In this view, the privileging by exposomics of the internal environment does not necessarily lead to the disregard of socio-political factors. This is where, however, an exploration of the political epistemology of analogical contemporary projects raises a series of challenges.

Epidemiological projects aimed at addressing the 'obesity epidemic' are a case in point. A political epistemology of these approaches underlines how methodological choices, at the level of research, define a space of possible political interventions. Doing so, it reduces the problem of nutrition to an individual issue, thereby invisibilising its socio-political determinants. This framing, here, is epistemically grounded on «evidentiary norms, reductionist underpinnings, and emphasis on causality and quantification» (Sanabria, 2016, p. 133). It therefore frames what counts as politically manageable through the «existing parameters of good science» (Sanabria, 2016, p. 135). These limitations are built from a myriad of methodological choices from the constitution of data

which, similarly to exposomics, «are not pre-determined by their objects of investigations» (Penkler, 2022, p. 5). At play as well is a drive towards political expediency and cost effectiveness, leading to a research that produces knowledge explicitly designed to be «pipeline amenable» (Landecker, 2013, p. 498): directly translatable into public health policies. This situation, also reminiscent of exposomics, favours the evidencing of individual, lifestyle interventions (despite their repeatedly recognised ineffectiveness) at the expense of possible alternative ways to understand and intervene on the factors driving obesity.

These tensions, visible also in adjacent fields such as obesity research, highlight the crossroads at which exposomics now stands. Faced with such challenges, our focus on situatedness and the integration of tools from *longue durée* history and political epistemology can also indicate possible futures of an approach such as exposomics. We outline three paths forward. The first, currently taken by exposomics researchers, is a continuous optimism about the newer technological developments. This process has been documented in the field of behaviour geneticists, where researchers have continuously responded to the recalcitrance of their object of research by investing «more money in higher-resolution technologies and to collect larger samples of research subjects» (Panofsky, 2015, p. 162). The recognition of complexity, in this field, is mobilised to «exonerate failure, justify intensified efforts, defend against charges of determinism, and project moderation and responsibility» (Panofsky, 2015, pp. 162-163). A continuous reliance on the latest technological developments, in this context, is seen as equally scientifically unproductive and a way of escaping accountability for the failure from previous investments to meet expectations. Applied to exposomics, this example suggests the risk of a possibly wasteful strategy of runaway technological investments repeatedly confronting the persistent wall of complexity.

Another strategy is to find alternative ways to embrace the complexity of the environment-health relations. One is evidenced by the *Whitehall studies*, which since 1967 have been investigating the prevalence of cardiovascular diseases and mortality rates among British civil servants (Marmot et al., 2002). This cohort study evidenced a social gradient of health: independently of the material conditions of the populations, an ascent in social status is associated with an improvement in health status (and conversely). These studies thereby clearly point to the detrimental health effects of social inequalities. The epistemological structure underlining its external validity is, however, much less streamlined than exposomics. It requires, above the epidemiological study, «marshaling a great deal of evidence of different kinds» which includes, among others, experimental primatology or comparative national health data in the context of drastic political regime change (Cartwright, 2006, p. 987). In other words, the success of the Whitehall studies is premised on its methodological opportunism in combining the available relevant evidence. This methodological opportunism exemplifies a different political epistemology – one that privileges pragmatic evidence integration over the pursuit of explanatory exhaust-

iveness. This strategy, however, poses a problem of standards of evaluation, since its critical assessment faces the absence of «experts on combining disparate kinds of evidence» (Cartwright, 2006, p. 987). In this view, an understanding of the health effects of the social environment seems to pose a trade-off between its epistemological feasibility and its possibility to be evaluated. This issue similarly applies to fields like social epidemiology, which try to ground their understanding of the biosocial dimension of health by garnering insights from «societal, ecological, spatiotemporal, geographic and historical» dimensions (Krieger, 2024, p. 291).

Finally, a third strategy is to defend a theoretical perspective that simplifies epistemological and political issues. This, in substance, is what partisans of Fundamental Cause Theory (FCT) are doing. Instead of proposing a perspective that identifies the deciphering of the minute details of how environments affect human health as its central priority, they explicitly embrace ignorance. FCT «essentially urges us to leverage certain social phenomena *because* of their multiplicity of unknown and changing effects» (Valles, 2019, p. 18). It orients research and interventions towards causes, such as poverty and stigmatisation, that «lay at the root of a plethora of very *different* effects» (Valles, 2019, p. 17). The idea, here, is to intervene in ways that would foster unknown effects of a predictable orientation. In this view, for instance, it is *not* necessary to decipher the totality of social and physiological effects associated with stigmatisation in a given context to know that, overall, a decrease in stigmatisation will have a positive health effect, in particular to the most vulnerable populations. Against the maximalist explanatory ambitions of exposomics, FCT is thereby grounded on the idea that «scrutinizing causal pathways is less promising when one is investigating the effects of a fundamental cause on a population» (Valles, 2019, pp. 19-20). That said, the validity and epistemological and ethical ramifications of this vision warrant further exploration.

Conclusions

More than a reaction to the excesses of gene centrism, exposomics lies at the tail end of a long history of approaches addressing the role of the environment on human health. Adopting this *longue durée* perspective, we contend, adds more than historical depth. It allowed us to emphasise the recurrence of a structure which interlinks theoretical beliefs, investigative priorities and a socio-political context. Identifying these components gives way to a complementary analysis that explicitly focuses on the political epistemology of exposomics. It allowed us to gather existing analysis on the approach to provide a normative assessment which conceived epistemological and ethical issues conjointly.

Overall, our analysis assessed two possible versions of exposomics, reflecting its oscillation between a claimed holism (for the integrative approach) and a privileging of exposures occurring at the internal level (for the internalist approach). From this initial disjunction, we identify two paths of downstream epistemological and political consequences. In the internalist approach, an increased attention to internal exposures leads to a lack of attention to the role of

collective, socio-political factors, and thereby leads to a reductive technicisation of public health. The integrative approach faces important epistemological challenges, notably (but not only) at the level of the constitution and analysis of data. Overcoming these challenges comes at the cost of confining the relevance of exposomics to environments amenable to the development of intensive data infrastructure, namely wealthy urban contexts. In this version, exposomics would thus become a science catering to the interests of the most affluent populations, thereby furthering socio-spatial inequalities.

These considerations lead us to reiterate the need for an increased reflexivity in exposomics. By this, we mean that its political epistemology, as an interlinked whole, needs clarification. This goes beyond, in our view, recent conceptual proposals that would allow to restore the truly holistic purview of exposomics, including the 'Socio-Exposome' (Senier *et al.*, 2016) or the recent emphasis on the conceptual importance of the 'biological capital' (Vineis & Barouki, 2022). As our longue durée analysis shows, aiming for a holistic science has always entailed, in practice, more or less conscious practical and political restrictions. The process of how such limitations come about – already and notably at the less visible level of data constitution – needs to be documented. Similarly, the epistemological consequences of the socio-political context motivating exposomics need to be made clearer: how is the identified tilt towards urban environments the product of political priorities? Could exposomics be shaped differently if it reflected alternative political priorities? Such tasks are necessary to allow the critical scrutiny, from scientists and non-scientists alike, of the concrete possibilities of such an ambitious endeavour.

A broader contextualisation of the exposome also allows drawing from a broader set of past and contemporary projects linking the environment and human health. This led us to identify three possible pathways for future exposomics: relying on the latest techno-scientific developments to overcome epistemic obstacles (a possibly wasteful strategy), adopting opportunistic and context-specific strategies for evidence integration (which poses issues in terms of external validity and evaluation) or giving up on holism by harnessing the unknown side effects of key causal factors (though its epistemological basis is currently underexplored). The identified challenges, we hope, not only clarifies possible developments for exposomics, but serves to illuminate the path of similar contemporary and future integrative projects at the intersection of environment and human health.

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– Exposome Research in the Perspective of *longue durée* Political Epistemology

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ABSTRACT
Exposomics has become a leading framework for examining how lifelong environmental exposures shape human health. We draw on historical and philosophical scholarship to situate its political epistemology and outline possible future paths. Historically, exposomics fits within a neo-Hippocratic tradition that links knowledge of environments and health to political priorities and interventions. Within this frame, two political epistemologies emerge: an internalist approach focused on biological tracking of environmental effects, and an integrative approach encompassing broader social and environmental layers. Both face notable epistemic and political limits. Drawing on analogical historical and contemporary cases, we identify three potential trajectories for exposomics – techno-solutionism, evidential pluralism, and fundamental-cause reasoning – each presenting distinct opportunities and challenges.

KEYWORDS
Exposomics; Integrated History and Philosophy of Science; Environment and health; Science and Policy; Population Health; Political Epistemology

SOMMARIO
La ricerca sull'esposoma nella prospettiva dell'epistemologia politica della 'longue durée'. L'esposomica è divenuta un quadro di riferimento centrale per studiare l'influenza delle esposizioni ambientali lungo l'arco della vita sulla salute umana. Integrando prospettive storiche e filosofiche, contestualizziamo la sua epistemologia politica e ne delineiamo possibili sviluppi futuri. Storicamente, l'esposomica si inserisce nella tradizione neo-ippocratica che collega le conoscenze su ambiente e salute a priorità politiche e interventi pratici. All'interno di questa prospettiva, distinguiamo due epistemologie politiche: un approccio internalista, incentrato sulla rilevazione biologica degli effetti ambientali, e uno integrativo, che amplia la considerazione anche a livelli sociali e ambientali in senso lato. Entrambe presentano limiti epistemici e politici rilevanti. Ispirandoci ad analoghi casi, sia storici che contemporanei, individuiamo tre traiettorie di articolazione possibili per la ricerca esposomica: tecnosoluzionismo, pluralismo evidenziale e ragionamento sulle cause fondamentali – e le diverse opportunità e sfide che comportano.

PAROLE CHIAVE
Esposomica; Storia e filosofia della scienza integrate; Ambiente e salute; Scienza e politica; Salute di popolazione; Epistemologia politica