

Article

Population Health Screening after Environmental Pollution

Alex G. Stewart ^{1,*}  and Ewan Wilkinson ² 

¹ College of Life and Environmental Science, University of Exeter, Exeter EX4 4QD, UK

² College of Medicine, University of Chester, Chester CH2 1BR, UK; ewilkinson@chester.ac.uk

* Correspondence: dragonsteeth@doctors.org.uk

Received: 20 May 2020; Accepted: 20 November 2020; Published: 24 November 2020



Abstract: Following environmental pollution exposure, calls to screen the population for disease or disease markers are often made. Population screening is a cross-sectional review of a population to find latent cases or biomarkers of disease that indicate the possibility of disease development; it differs from environmental screening or an epidemiological survey. Recognized standard approaches have been developed over 60 years to ensure quality and effectiveness in complex programs. We surveyed the literature for papers on health screening following environmental exposures and checked them for reference to accepted criteria such as those of Wilson and Jungner. We applied these criteria to three situations covering source/hazard (arsenic contaminated land), pathway/exposure (radiation release), and receptor/disease (lead poisoning). We identified 36 relevant papers. Although across the papers the whole range of criteria were addressed, no paper or program utilized recognized criteria. Issues and gaps identified included limited strategic approaches, lack of treatment, environmental prevention being seen as the screening outcome instead of treatment of identified individuals, and programs which did not fit the World Health Organization screening description. Robust discussion in the literature is needed to consider the organization and role of health screening following environmental exposures.

Keywords: chemical pollution; mental stress; environmental toxins; potentially harmful elements; principles of screening; Wilson and Jungner; arsenic; lead; radiation

1. Introduction

Pollution is the largest environmental cause of premature death and disease in the world today, with a greater impact on global health than cancer. In 2015, it caused an estimated 9 million premature deaths (16% of all deaths worldwide) and the loss of 268 million disability adjusted life-years (DALYs—see Box 1) [1]. Air pollution causes 70% of the pollution-related disease burden, with 1.6–4.8 million premature deaths annually worldwide, predominantly from residential heating and cooking in Asia [2–4]. The enormous number of contaminated land sites in low- and middle-income countries from industrial and commercial activities, large and small, put the health of possibly more than 200 million people at risk [2]. There are an estimated 0.5–0.7 million deaths per year from contaminated soil, heavy metal and chemical exposure combined, with lead on its own contributing another 0.5 million deaths [1]. Industrial and development-related pollution (including electricity generation, mechanized agriculture, and petroleum-powered vehicles) has rapidly increased across the globe, with a resulting continuous increase in pollution and premature deaths [1]. The top 10 contaminating industries (at all scales) account for 7–17 million DALYs in low- and middle-income countries, with >32 million people at risk in the industries which span 150,000 sites in about 50 countries [5].

This increase of pollution and resulting ill-health has been ascribed to the current, unsustainable, economic paradigm which gives little heed to the consequences of recklessly exploiting natural and human resources [6]. Modelling indicates that premature mortality due to outdoor air pollution could

double by 2050 [2]. Out of 140,000+ new chemicals since 1950, there are 5000 chemicals which are most widely dispersed, and which are responsible for adverse human exposures on a global scale. Environmental exposure of selected chemicals was calculated to cause 8% of all pollution deaths and 6% of the global burden of disease (DALYs) in 2011, which almost certainly underestimates the overall contribution of chemicals to ill-health and disease [1].

Box 1. Definitions and descriptions.

DALY: Disability adjusted life years—the sum of years of potential life lost due to premature mortality plus the years of productive life lost due to disability. (World Health Organization. Mental Health. DALYs/YLD definition. 2020. https://www.who.int/mental_health/management/depression/daly/en/).

PREVENTION: Primary prevention refers to actions aimed at avoiding the manifestation of a disease (this may include actions to improve health through changing the impact of (environmental) determinants on health). Secondary prevention deals with early detection when this improves the chances for positive health outcomes (this comprises activities such as evidence-based screening programs for early detection of diseases). (World Health Organization. About us. Health promotion and disease prevention through population-based interventions, including action to address social determinants and health inequity. <http://www.emro.who.int/about-who/public-health-functions/health-promotion-disease-prevention.html>).

SCREENING: The presumptive identification of unrecognized disease in an apparently healthy, asymptomatic population by means of tests, examinations or other procedures that can be applied rapidly and easily to the target population. A screening program must include all the core components in the screening process from inviting the target population to accessing effective treatment for individuals diagnosed with disease. Screening is a process, beginning with an invitation to participate and ending with treatment for appropriately identified individuals. Compared to early diagnosis, cancer screening is a distinct and more complex public health strategy that mandates additional resources, infrastructure and coordination. Screening programs should be undertaken only when their effectiveness has been demonstrated, when resources are sufficient to cover nearly all of the target group, when facilities exist for follow-up of those with abnormal results to confirm diagnoses and ensure treatment and when prevalence of the disease is high enough to justify the effort and costs of screening. (World Health Organization. Cancer. Screening. 2020. <https://www.who.int/cancer/prevention/diagnosis-screening/screening/en/>).

SENSITIVITY and SPECIFICITY: Sensitivity is the proportion of people with a disease who have a positive test, i.e., are correctly diagnosed; specificity is the proportion of people without the disease who have a negative test, i.e., are correctly eliminated from having the disease. (Cochrane UK. <https://uk.cochrane.org/news/sensitivity-and-specificity-explained-cochrane-uk-trainees-blog>).

SYNDROME: A group of symptoms which consistently occur together, or a condition characterized by a set of associated symptoms.

Children under the age of 15 years bear over half of the overall burden of disease from pollution [7]. Even extremely low-dose exposures to pollutants during windows of vulnerability in utero and in early infancy can result in disease, disability, and death, both in childhood and later in life [1]. Exposed girls can transmit resulting health disorders to their own children and grandchildren (e.g., [8,9]). Childhood lead poisoning remains an international public health problem; 97% of children exposed to toxic levels of lead live in low- and middle-income countries [10], with lifelong adverse neuropsychological consequences [11,12]. Exposure of children to lead still occurs in high-income countries, from contaminated land and old paint, amongst other sources [10,11].

The effects of chemical pollution on human health are poorly defined and it is almost certain that the burden of disease from chemical pollution is underestimated. Fewer than half of the new chemicals introduced since 1950 have any toxicological testing [1], although a few high-income countries have recently introduced rigorous pre-market evaluation of new chemicals (for example, [13]). In addition, the anxiety arising from contamination situations or chemical exposure and the potential for resulting ill-health consequences can be a major health issue in its own right. Anxiety can often cause more ill-health than any actual physical disease arising from the exposure, as it may affect more people than those deemed at risk from the contamination [14,15]. It remains an area that would benefit from further investigation.

2. Background

Following the identification of an exposure to environmental pollution, it can be appropriate to consider whether it is possible to identify those people who may be developing disease, in order to give them early treatment and reduce morbidity and mortality. Population screening (see Box 1) uses an appropriate test to detect early disease in individuals in a given population; it is cross sectional in time, although it may be repeated later [16]. Since population health screening finds possible and actual cases of disease (Figure 1), it differs from surveillance of disease, which is a longitudinal, continuous review of disease in a population to elucidate the prevalence, incidence, and natural history of the variables under study. Surveillance operates at a population, not an individual, level. Screening also differs from impact assessment, whether environmental or health, since these are risk assessments and not designed to identify individuals with disease. Equally, it differs from the monitoring or screening of potential pollutants in the environment.

Public health screening of populations has developed from small origins in industry for occupational diseases in the 1950's (often due to environmental toxins) to cover a complex range of diseases, tools, and programs which have been put into place for the general population (or defined sub-sections) in high-income countries [16–18]. We do not consider occupational health screening further in this paper. Current examples of population screening programs can be illustrated by the range of screening in the UK at specific times in life, e.g., pregnancy, at birth, men aged 65, or for specific diseases, e.g., diabetic eye disease, cervical or breast cancer, and bowel cancer [19].

Early in the burgeoning variety of population health screening programs, a seminal report was produced in 1968 by two leading experts, Dr James Maxwell Glover Wilson and Dr Gunnar Jungner, following a commission from the World Health Organization. Wilson was Principal Medical Officer in the United Kingdom's Ministry of Health, while Jungner was Chief of the Clinical Chemistry Department, Sahlgren's Hospital, Gothenburg, Sweden. Together, Wilson and Jungner reviewed population health screening and enunciated 10 criteria to be considered when deciding if a population screening program should be started [17] (Figure 2).

These 10 criteria have stood the test of time [20], being seen as the gold standard when making decisions about any screening program [21,22]. They stand behind the World Health Organization's definition of screening (Box 1). However, they have also been criticized as being too theoretical for neonatal screening [23], or difficult to assess in a consistent manner [24,25], since they are not wide enough to capture all the various aspects of modern screening programs [26]. Consequently, several authors have elaborated on these influential ideas for specific health situations, such as pediatrics [24] or genetic disorders [25], although most of the changes are around the practical issues of screening, not the science (Table 1). Many of the newer criteria reflect trends that have reshaped Western medicine and Western society over the 50 years since the publication of the original criteria, as much as they reflect advances in science [21]. Some reports have grouped the criteria, the most useful classification being comprehensive, and easy to remember and apply: (1) the condition to be screened for, (2) the test to be used, (3) the program to be developed, and (4) the treatment of (or intervention for) positive and negative cases (Figure 2) [27].

The application to environmental situations remains unclear. There is very little in the literature on population health screening following a pollution event or environmental exposure, despite a common question by those responsible for assessing the health impact being, "Can we screen an exposed population for relevant disease in this pollution situation?"

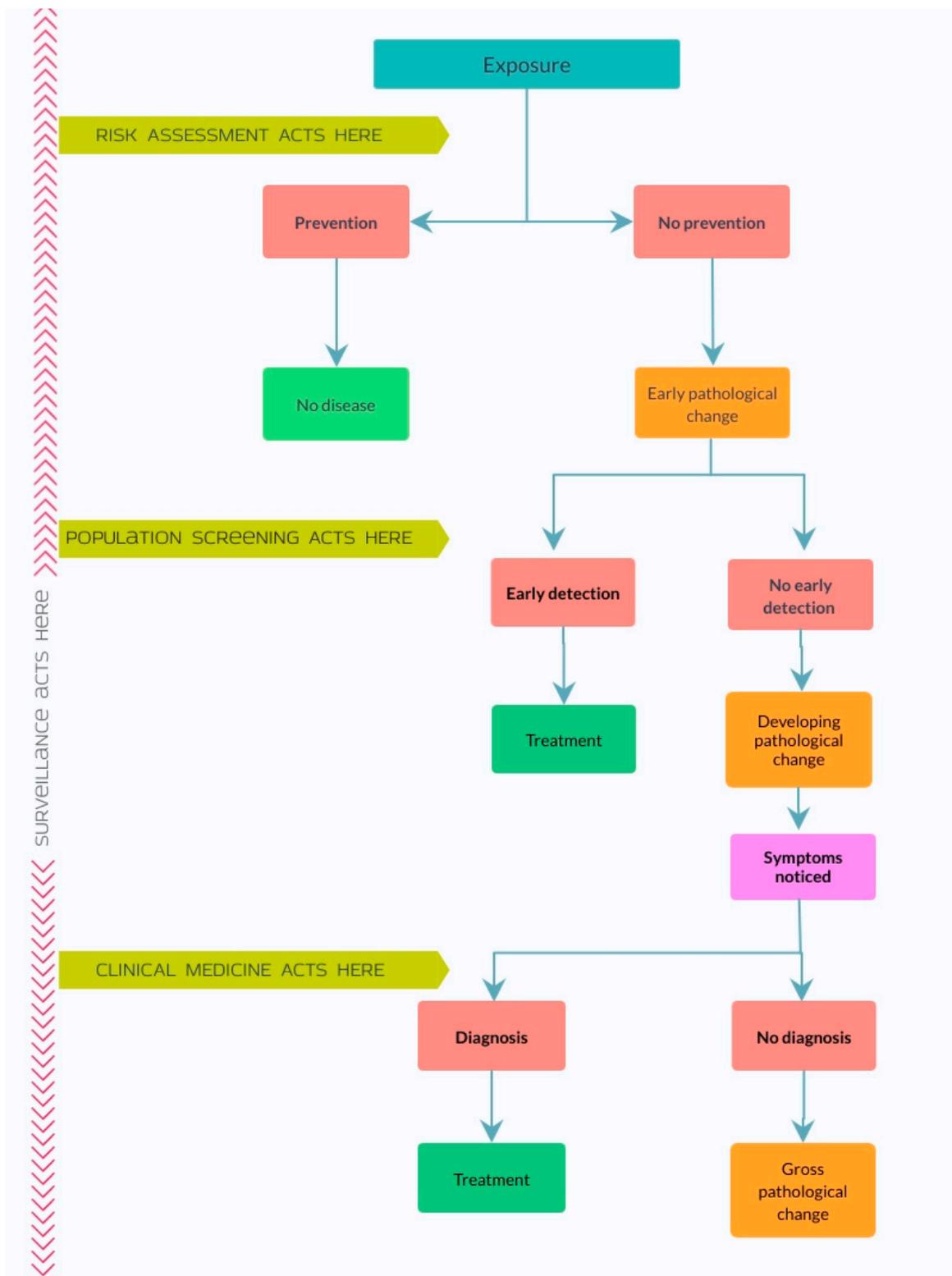


Figure 1. Case finding and disease progression after environmental exposure. Developed from [17].

We aimed in this study to identify good practice in the implementation or description of population health screening related to pollution situations, as determined by the application of recognized criteria to organize and assess such programs. Our research questions were, what can be learned from a literature search about the use of a population health screening approach when environmental pollution is being investigated? Do the approaches used fit with accepted screening criteria? Were any gaps in knowledge or practice identified?

In order to identify these gaps, we intended to identify relevant criteria and programs and apply them to three environmental situations that we have met in our public health practice and which reflect the three aspects of the well-recognized source-pathway-receptor approach to environmental issues. This environmental approach is parallel to the health perspective of looking at the hazard, the resulting exposure, and possible ensuing disease or syndrome [28].

Table 1. The changing numbers of population screening criteria 1968–2018, in groups from [17] showing adaptations to specific situations while validating the original approach.

Date	Total Principles	Condition	Test	Program	Treatment	Source
1968	10	3	2	3	2	Original formulation [17]
1998	19	3	4	9	3	UK general screening principles [27]
2004	20	3	5	8	4	Workshop on genetic immune-deficiencies [25]
2008	20	3	2	13	2	Synthesis of 50 lists covering 40 years [21]
2018	12	3	2	6	1	Qualitative review to consolidate 40 lists [20]

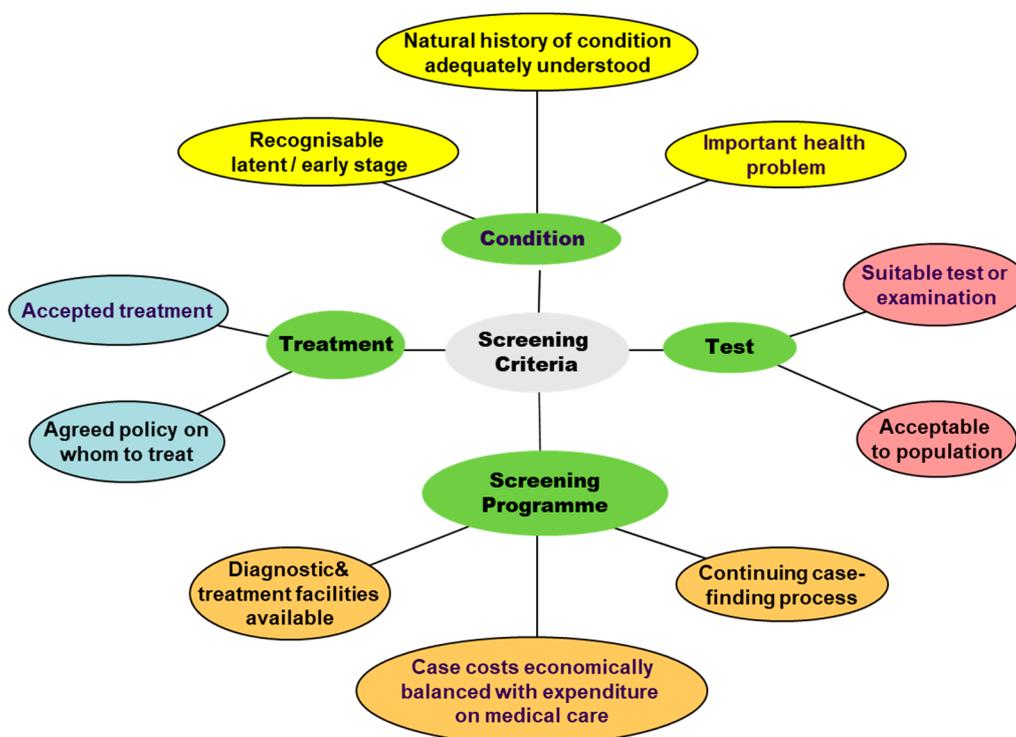


Figure 2. The 10 criteria for a health screening program developed by Wilson and Jungner (outer ring), in four recognized groups. Developed from [17,27,29].

3. Methods

We undertook a literature review in PubMed (<https://pubmed.ncbi.nlm.nih.gov/>) using major MESH (Medical Subject Headings) terms, “Environmental Exposure” or “Environmental Pollution” and “Mass Screening” or “Diagnostic Screening Programs”. From this initial list, we took an iterative approach, initially identifying through the title and abstract any papers in English which described a screening program centered around classical air, land, or water pollution. We read the text of any relevantly titled paper without an abstract. We excluded papers which were not focused on the environment and health (e.g., lifestyle issues such as tobacco smoke, alcohol or drugs, exposure scenarios without specific health outcomes, occupational exposures, and relevant screening of the environment for hazardous chemical contamination but without relevant health screening). We did not limit the search to any particular years: The term “mass screening” was added to PubMed in 1968, “environmental exposure” and “environmental pollution” were introduced in 1974, while diagnostic screening programs was added in 2019.

Secondly, we searched the full text of the identified papers for any reference to screening criteria, either the 10 seminal criteria by Wilson and Jungner [17], or another derived set of criteria related to that original list, or to any pre-selected and objective criteria [26], or the four groups as in [27,29] (Figure 2). From this, we expected to develop a list of criteria that were considered relevant to environmental situations.

Thirdly, we assessed the use and understanding of the role of objective criteria in the screening programs discussed in the scientific literature. Accordingly, we undertook a thematic analysis by reviewing the papers again and identifying the major themes, whether explicit or implicit, in each paper according to the identified objective criteria. We initially intended to use the criteria we found in the literature but where there were none, we resorted to the original 10 criteria of Wilson and Jungner. We used these classical criteria rather than any others because of their acknowledged utility and foundational thinking. We considered using other criteria developed from them, as per the background above (Table 1), but decided that the original 10 criteria were simple and comprehensive enough for an initial look at environmental pollution. Subsequent criteria were developed for specific health settings which were not believed to be relevant to this study. Furthermore, we counted the coverage of the four recognized groups (condition, test, program, and treatment: Figure 2) in each paper.

Once we had completed the literature review, we applied these screening criteria to three environmental pollution situations which we have encountered, to assess how these criteria supported making decisions on screening programs relevant to environmental pollution situations and to identify gaps in knowledge or action that need addressing.

Using the source-pathway-receptor model, which has been beneficially linked to public health approaches to environmental issues [28,30], we identified areas for further consideration: (1) source/hazard: Land contaminated by arsenic, (2) pathway/exposure: A radiation release, and (3) receptor/disease: Lead poisoning in children. We recognized that all three situations need all three components of the source-pathway-receptor linkage to result in disease. However, we considered this a useful approach to explore the utility of screening criteria following environmental pollution. This is because the initial presentation of a contamination situation and its impact on health may be due to the hazard, the exposure, or the resulting disease (or suspicion).

This was a descriptive study; we did not attempt to undertake any statistical analysis. Such analysis was unsuited to the questions we were asking and, also, few papers presented any quantitative data that was comparable with data in other papers.

4. Results

The literature search on 7th March 2020 identified 242 possible papers from 1962 to 2020. Following review of the title and abstract we identified 36 papers from 1979 to 2019 on environmentally relevant population health screening programs.

We reviewed the text of the 36 papers (Table 2) to identify references to objective screening criteria. No paper used recognized screening criteria to assess the utility of an environmentally-relevant, population health screening program, whether the original Wilson and Jungner criteria or any others. Indeed, we were unable to identify any routine public health program of health screening of any population for environmentally induced disease anywhere that clearly utilized recognized criteria. We were unable to find any published schema related to screening which we could use to classify the papers.

Accordingly, our thematic analysis was based on the original Wilson and Jungner criteria (Table 2) and the four UK screening groups (condition, test, program, treatment) (Figure 2). We found only one paper, from 2018, which gave adequate information on all 10 criteria in all four groups; only three other papers (from 1994, 2003, 2008) also covered the four screening groups but with less than full coverage of the criteria. The fullest paper focused on patient awareness of screening for chronic kidney disease in Japan, whether of environmental origin or from other causes such as diabetes mellitus or hypertension, rather than the screening program itself [31] and so was not directly discussing health screening under objective criteria.

Three other papers, all from the USA, covered the four groups, although missing some of the 10 criteria. One, from 2008, addressed pediatrician's attitudes and beliefs around environmental hazards [32]. Another, from 2003, considered the need for a reduction in the blood lead intervention level [33]. The third paper, from 1994, was a brief strategic look at screening and health risk assessment related to environmental situations; this paper came the nearest to a full, albeit very short, discussion of screening as envisaged by the recognized international approach encouraged by the World Health Organization. The first two of these papers covered only one criterion from each group, while the third was weak in discussing the health condition to be screened for, perhaps not surprising in a broad-ranging strategic paper.

As mentioned above, the information on screening criteria was limited in most papers and only some of the 10 criteria of Wilson and Jungner were covered: 16 (44%) covered one criterion, nine (25%) two criteria, and five (14%) three criteria. One paper, a 1988 commentary on the then US lead screening program, did not consider any criteria in any form [34]. Although one paper mentions screening criteria in the title, these criteria concern choosing children for the study; the paper does not discuss screening criteria in the sense we used [35]. Fifteen (42%) papers considered the condition, 18 (50%) the test, 17 (47%) the program and eight (22%) the treatment (Table 2).

Twenty (56%) of the papers were concerned with the health results of lead exposure (13 (36%) came from the USA). The other papers covered a wide variety of environmental and health situations (14 topics excluding lead), none with more than two papers.

The USA has had variable success in running population-based health screening for lead poisoning in children [36–38]. The current verdict on the US program is unclear about how effective screening for elevated lead levels of asymptomatic children actually is in protecting children from either the health effects of lead exposure, or from ongoing exposure [38]. Furthermore, the US program, although the best described and developed program we found, concentrates on prevention. Thus, it does not fit the WHO definition of a screening program, which is concerned with early identification of disease with appropriate treatment (Box 1).

Since we could find no examples in the literature of using screening criteria derived for such situations in assessing actions for environment pollution, we applied Wilson and Jungner's original criteria to the three scenarios ((1) land contaminated by arsenic: Source/hazard, (2) a radiation release: Pathway/exposure, and (3) lead poisoning in children: Receptor/disease). The results are shown in Table 3. The most important issue we realized was the final criterion, "Is there suitable treatment

available?'. With no simple treatment options following arsenic contamination, and reduction in exposure to lead being the main response to elevated blood lead levels, the benefit of implementing screening programs in these situations remains questionable. This is supported by the literature review where none of the diseases described are easily amenable to a treatment which will make a substantial difference to the life of the patient.

Other issues identified included diagnostic methods, timing and tests used, and the lack of a strategic approach to population health screening in environmental pollution.

The issue of variable results from the diagnostic methods used in the USA lead screening program was noted in the literature, arising from self-reporting by the potentially exposed community [39] or questionnaires completed by patients in clinics [40–42]. In another, non-lead, study, the method was obstetricians questioning of patients: Older obstetricians found it easier to question patients about a variety of environmental exposures relevant to pregnancy and fetal development than obstetricians who were more recently qualified. However, the approach appeared somewhat haphazard and did not seem to have a robust structure [43].

The diagnostic test(s) used for the disease under consideration in a screening program is of vital importance. Many papers discussed tests (Table 2), but there was little discussion of the sensitivity or specificity (Box 1) of the tests, an important issue when examining asymptomatic people. Biomarkers of early disease, before clinical symptoms arise, need to be clearly identifiable. It is worth noting that specific biomarkers of the relevant disease in the latent phase do not exist at the moment for most environmentally-induced conditions (Table 3), a point largely ignored in the papers reviewed. Blood lead level is one of the best recognized biomarkers for exposure (not necessarily of disease), whether current or in the past, and was the most discussed (11 papers).

Monitoring of radiation levels of exposed people is carried out too early to identify latent disease. Rather, it identifies exposure to radiation and its main benefit is to assure the worried well that they have not been exposed to significant radiation from the incident. Anyone with significant exposure can be followed up through a register [44,45]. However, this is monitoring, not screening. Post-radiation monitoring is another example of a program that some might consider to be screening but does not fit the definition.

The lack of a strategic approach to screening programs was seen in the limited number of papers on any subject other than lead poisoning and in narrow the focus on subsections of the four groups or 10 criteria (Table 2).

Further to these three important points (lack of treatment, diagnostic issues, and strategic approaches) specific gaps in knowledge relevant to screening programs can be further identified through the worked examples in Table 3. However, any such gaps are secondary to the lack of a systematic and strategic approach to screening and the lack of suitable treatments, which render programs ineffective and make any other knowledge and practice gaps of lesser, even limited, importance. Accordingly, we did not pursue these further at this time.

Table 2. Coverage in the literature review papers, within four recognized screening groups, of the 10 Wilson and Jungner screening criteria [17], showing the number of criteria covered and the group into which they fall.

Year	Focus of Paper	Condition	Test	Program	Treatment	Number of Criteria Groups	Total Criteria Quoted	Source
2019	Review of Pb program. USA			1	1	2	2	[38]
2018	Obstetrics screening for environmental exposure. USA	3				1	3	[43]
2018	CKD screening. International	3	2	3	2	4	10	[31]
2017	COPD. Japan		1			1	1	[46]
2017	Legal; harm/benefit. USA	3			1	2	4	[47]
2015	Pre-pregnancy CH ₃ Hg. Canada			1		1	1	[48]
2015	Predicting BLL >50. France			1		1	1	[35]
2012	Predicting BLL. NV, USA			1		1	1	[42]
2012	Predicting BLL and costs. MI, USA		1	2		2	3	[39]
2011	Rapid radiation test. NYC, USA		1			1	1	[49]
2009	Determining Pb exposed population. GA, USA			1		1	1	[50]
2009	Bladder Cancer. USA	2				1	2	[51]
2008	Radiation risk communications. TX, USA			1		1	1	[52]
2008	Pediatricians' attitudes & beliefs. MN, USA	1	1	1	1	4	4	[32]
2008	Not attending for BLL, NSW, Australia		1		1	2	2	[53]
2007	Biomonitoring concentrations. USA		1			1	1	[54]
2007	Predicting BLL >100. France			1		1	1	[55]
2007	Health outcomes of war. Iran	1				1	1	[56]
2004	Indian children's lead. USA	1				1	1	[57]
2004	Pb epidemiology in children. Chicago, USA	1	1			2	2	[58]
2003	BLL levels. USA	1	1	1	1	4	4	[33]
2002	Scoliosis screening. Greece	2				1	2	[59]
2001	Dioxin. Japan		1			1	1	[60]
2001	Screening age >36 m ineffective; Pb. NY, USA	2		1		2	3	[61]
1999	Pb costs. MN, USA		1	1		2	2	[62]
1999	Screening women for Pb. NY, USA		2			1	2	[63]
1998	Comment on CDC Pb guidelines. USA					0	0	[34]
1997	Ease of blood testing, Pb. NY, USA		1			1	1	[64]
1996	Telephone review Pb screening. USA			1	1	2	2	[65]
1994	Screening tool, Pb. WI, USA		1			1	1	[40]
1994	Predicting BLL. CA, USA		1	1		2	2	[41]
1994	Strategies for health screening. USA	1	2	2	2	4	7	[66]
1993	Pediatric BLL pilot. AK, USA	1				1	1	[67]
1992	GIS for Pb screening. USA			1		1	1	[68]
1984	Dioxin pilot. MO, USA	2	1			2	3	[69]
1979	Testing for Cd. Japan	2	1			2	3	[70]

Notes: BLL = blood lead level; CDC = Centre for Disease Control; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; GIS = Geographical Information System. Other abbreviations are elements or states.

Table 3. Using population screening following environmental contamination: Three worked examples assessed against Wilson and Jungner [17] criteria.

Criterion [17]	Soil Arsenic	Radiation Exposure	Childhood Lead
<i>Condition</i>			
Natural history of condition adequately understood	Not adequately	Well understood	Yes, clear links between BLL and disease
Important health problem	Cancers and disfiguring skin problems can result	Politically, socially, medically important	Lifelong neuropsychological effects
Recognizable latent/early stage	No single identifiable early condition; markers sensitive but not specific for environmental source	Main thrust of program is to reassure the “worried well”. Latent stage of disease comes much later than the “screening”	Unclear if low BLL indicates future high BLL or just low exposure
<i>Test</i>			
Suitable test or examination	Sensitive, but not specific as to source of As	Yes, but detects contamination by radiation, not disease	BLL
Acceptable to population	Blood, urine, hair sampling are variously acceptable	Yes	Blood test; not always acceptable to children
<i>Program</i>			
Ongoing case-finding process	Needs commitment and resources	Resource intensive initially	Needs organizing centrally. Needs commitment and resources
Case costs economically balanced with expenditure on medical care	Unknown	No, but high level of reassurance can be given	Yes
Diagnostic & treatment facilities available	No	Yes, for contamination	Yes
<i>Treatment</i>			
Accepted treatment	No	Depends on resulting disease	Limited to high BLL
Agreed policy on whom to treat	No	Well worked out for contamination	No; focus is on prevention not treatment

BLL = blood lead level.

5. Discussion

We searched the scientific literature for appropriate ways to undertake population health screening in environmental pollution situations, using accepted screening criteria. To our knowledge, this is the first time that such approaches have been reviewed in the literature. We found no environmentally related programs which overtly discussed the 10 seminal criteria from Wilson and Jungner's report [17] or other accepted criteria.

We found important gaps: Firstly, there is a current lack of treatment for any resulting disease in three representative scenarios covering source (hazard), pathway (exposure), and receptors (syndrome or disease). This is in line with the fact that few (8; 22%) of the papers we found covered treatment. This was less than half of the number of papers discussing the test (18; 50%) or the program (17; 47%) and much less than the papers discussing the condition (15; 42%). This raises questions about the utility of current screening approaches to the detection of disease arising from environmental pollution. What is the point of screening if there is no answer for the patient for their identified health issues? However, recent advances in early diagnosis and simpler treatments suggest that this lack of current treatments is not a fatal flaw for pollution-related health screening programs; it is possible that relevant tests and treatments will be developed that enable such screening programs to be developed for diseases related to environmental exposures.

The need for good biomarkers of disease is crucial. Finding suitable biomarkers to identify early disease resulting from arsenic contamination can be problematical [71,72]. Few biomarkers are as well understood as blood lead level, a clear marker for lead exposure having occurred at some point, whether current or in the past. The concentration of blood lead can be a pointer to the particular disease expected (low lead levels affect neurocognitive development; higher concentrations give anemia or gastrointestinal problems), but there is no treatment at the lower concentrations, only removal of source. At higher concentrations (>45 µg/dL), chelation therapy may be used, but the aim of this treatment is to reduce the high blood lead level; it does not directly address the resulting disorders.

Secondly, and perhaps more importantly, we found limited discussion around how to systematically organize and evaluate such screening programs, although the variety of issues covered is encouraging. The lack of reference to, or engagement with, the extensive health screening literature was disappointing, showing an important lack of appreciation of the need for a strategic approach to program planning. Since the publication of the seminal criteria [17] there has been ongoing debate and refinement of the approaches to the organization of health screening, with aspects such as quality control, economics, and outcomes being monitored and improved. Furthermore, the extensive enlargement across a variety of health fields of the Wilson and Jungner criteria (as illustrated in Table 1) to produce relevant criteria that can be used objectively to structure and evaluate programs has no parallel in the environment—health interface, leaving plenty of room for development.

Only four papers covered all four of the screening groups (condition, test, program, and treatment), suggesting that few authors, although writing about their own screening situation, were aware of the abundant screening literature. Such a situation might be due to the compartmentalization of science with increasing knowledge on the one hand, and the pressure on outcome measures in programs on the other, although there may be other as yet unrecognized reasons.

Given that population health screening has a long and successful history, and pollution is an important and worldwide cause of morbidity and mortality, these gaps are disappointing. Population screening programs are recognized to need a structured approach to ensure that the program is wide and informed (Box 1) [21,22,73,74]. The scrutiny of the US lead screening program, raising questions about the efficacy of screening asymptomatic children [38], is an example of much needed discussion. The succinct paper by Wallace and Murray [66] covers much of the ground for discussion without focusing on any specific disease outcome from environmental pollution. That paper appears to be as unknown as the more general screening literature but should be recommended reading for anyone considering health screening related to pollution.

The Wallace and Murray paper from 1994 focused on prevention in contradistinction to the focus of extant health screening programs on early diagnosis and treatment. These programs often focus on a single disease, e.g., breast cancer or aortic aneurysm. The issue in many of the screening programs is that, while the natural history (progression) of the disease is understood, the etiology is unknown. Treatment, then, becomes all that can be offered, and the earlier the better. However, in environmental pollution, the exposure is known or suspected, even if knowledge about any latent period of the disease, during which early diagnosis becomes possible, is unclear. As a result, the focus of response in environmental situations should be different from the more medical situations. For example, lead screening programs in children aim to identify exposed children and respond to the exposure, as well as to the child with raised blood lead levels.

This raises the question: Is the current WHO definition of health screening (Box 1) too narrow and medically focused? Should it include prevention as well as treatment as the outcome? Or, if not prevention, then, as in lead, a recognition of exposure and the consequent removal of the source or the pathway, which is helpful if not curative. Discussion around the role of screening in environmental pollution situations could help widen thinking about screening in the health community.

Such a shift in thinking about screening outcomes needs a corresponding move concerning the underlying approach to health issues. The medical model of health concentrates on diagnosis and treatment of disease and still plays a major role in the design and delivery of health services and the understanding of health in many communities. It has been criticized for its limited approach, ignoring social, economic, and environmental factors in the causation and control of ill-health [75]. Public health has moved to a bewildering array of 21 or more different versions [76] of a wider socio-economic [77]/socio-ecological [78]/socio-environmental [79] model. These models take into account a broader range of the issues determining health. Nevertheless, the role of the environment, whether natural or man-made, is often underestimated or even overlooked, with the focus primarily on lifestyle choices. Environmental pollution is not a choice; issues of pollution are pervasive while the resulting exposures are only slowly being quantified and acknowledged [79] by the wider community [1,2,4,5,80].

Pollution often arises from a mixture of chemicals, giving multiple and interacting exposures, from which a variety of diseases may result. While this is recognized within the environmental science community, the effect of chemical mixtures remain less explored on the health side [81,82]. Similarly, there can be either acute or chronic exposures to a pollutant, which may give rise to different health outcomes. Screening for some health condition needs to be repeated on a regular basis, (e.g., breast cancer screening), since there is the possibility of developing disease after the initial screening. This may be equally important in pollution situations. All these issues are further reasons to generate discussion across the environmental-health border, involving both communities.

The US lead screening program highlights the need for prevention [38]. Perhaps the definition of a screening program should be expanded to include prevention rather than a sole focus on treatment as the outcome of the program. However, screening for prevention is more complex than screening for early disease detection. Screening for prevention needs to include screening of the environment for hazardous chemical contamination, as well as population health screening to find early, treatable disease arising from such exposure. Risk assessment and risk management of the source (hazard) and pathway (exposure) to reduce possible exposure is as important as health screening for resulting disease (receptor). Further, health screening should never replace primary prevention (Figure 1) (Box 1). Health screening is, at best, a form of secondary prevention (Box 1). While prevention can bring about greater health benefits than the early identification of disease, both can be beneficial but contribute in different ways.

Of course, science is not everything, even in screening. Policy often trumps science and there may be ethical decisions beyond the relevance of screening criteria that need to be taken into account [83,84]. Values will always be more influential than evidence in deciding policy [85]. Nevertheless, this does not justify not using the science when it is available.

The strengths of this study include being the first to apply widely recognized criteria on screening to pollution-related health situations. We used multiple methods (triangulation) to develop a comprehensive understanding and increase the reliability of our findings. The literature was examined for mention or discussion of objective screening criteria in the design or operation of the program, a thematic analysis of papers against recognized screening criteria was undertaken, and we applied recognized criteria to the three case studies covering the source-pathway-receptor approach to pollution. These differing approaches consistently revealed basic weaknesses in environmentally related population health screening approaches, increasing the dependability of the conclusions.

Weaknesses of the study include the limited literature review of screening programs, due to the constraints of resources and the Covid-19 situation. Grey literature was not searched; it is possible that there are screening programs adhering to standard approaches, but which have not been recorded in the academic literature. The subject needs a wider and more detailed literature review than we were able to undertake.

6. Conclusions

We recommend that health screening programs related to environmental pollution need to be more systematically developed to ensure that they achieve their intended outcomes. They should be guided by appropriate criteria, which may need to be further developed for pollution situations. They need to be consistent with wider health policy issues. They should not expect clinicians to ask relevant questions without careful planning and evaluation of the whole program [32,43].

We therefore recommend that a vigorous discussion is undertaken across the public health and environmental communities about the use of screening in the management of pollution events. This has been done for other health issues arising from specific determinants (e.g., genetic diseases [25,86]) or in specific situations (e.g., pediatric/neonatal screening [24]). Such a discussion needs to happen before any further identification of knowledge gaps; indeed, such a discussion would help identify the gaps in more detail. The identification of gaps would also clarify areas for further research, whether source, pathway or receptor, condition, test, program or treatment [66].

This discussion should include an assessment of whether or not, or when, such programs are needed, the criteria for organizing and evaluating the programs, the information needed to run a useful program, the strength of evidence on which to base a program (including evidence of sensitivity and positivity of the tests and efficacy of the treatment), agreed outcomes, whether treatment or preventative activities, and defined strategies for dealing with people with positive or negative tests.

Since the potential number of environmental scenarios is large, it would be a mistake to attempt to develop a stand-alone program for each chemical or disease. Rather, a strategic approach should take into account different sources/hazards, pathways/exposures, and receptors/diseases or syndromes to help guide further relevant and useful programs. However, any generic approach should be flexible enough to be adapted in specific situations. Wilson and Jungner wrote, "In theory, screening is an admirable method of combating disease . . . in practice, there are snags", and "[screening] is far from simple though sometimes it may appear deceptively easy" [17]. This is still true.

Sir Muir Gray, former director of the UK National Screening Committee, wrote with colleagues, "All screening programmes do harm; some do good as well, and, of these, some do more good than harm at reasonable cost. The first task of any public health service is to identify beneficial programmes by appraising the evidence. However, evidence of a favourable balance of benefit to harm in a research setting does not guarantee that a similar balance will be reproduced in practice, so screening programmes need to be introduced in a way that allows their quality to be measured and continuously improved." [74].

An evaluation of the usefulness of implementing a population health screening program after environmental exposure to pollutants is urgently needed, through a wider discussion in the wider public health community, including toxicologists, epidemiologists, clinicians, policy makers, and environmental scientists. Toxicologists and clinicians understand patients and their diseases,

but environmental scientists understand the source-pathway-receptor approach to environmental situations that parallels the hazard-exposure-disease pathway that health professionals are used to. The standard approaches to developing and running a screening program need to be evaluated in the light of pollution exposures. If such an approach is beneficial it would reduce the ill-health from an exposure. If it is not, it can then be discarded, saving time and resources.

Author Contributions: A.G.S. conceived and wrote the first draft; E.W. and A.G.S. then revised the paper and agreed the final version. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Acknowledgments: A.G.S. acknowledges the support of Khaliq O Malik, and early discussions with Hilary Thurston on applying screening criteria to environmental situations. The perceptive comments of four reviewers are also very much appreciated and helped develop our thinking, as well as the paper.

Conflicts of Interest: The authors declare no conflict of interest.

References

- Landrigan, P.J.; Fuller, R.; Acosta, N.J.R.; Adeyi, O.; Arnold, R.; Basu, N.; Baldé, A.B.; Bertollini, R.; Bose-O'Reilly, S.; Boufford, J.I.; et al. The Lancet Commission on pollution and health. *Lancet* **2017**, *391*, 462–512. [CrossRef]
- Lelieveld, J.; Evans, J.S.; Fnais, M.; Giannadaki, D.; Pozzer, A. The contribution of outdoor air pollution sources to premature mortality on a global scale. *Nature* **2015**, *525*, 367–371. [CrossRef] [PubMed]
- Li, X.; Jin, L.; Kan, H. Air pollution: A global problem needs local fixes. *Nature* **2019**, *570*, 437–439. [CrossRef] [PubMed]
- Finch, C. *The Role of Global Air Pollution in Aging and Disease*, 1st ed.; Academic Press: London, UK, 2018; ISBN 978-0-12-813102-2.
- Pure Earth and Green Cross Switzerland. *The World's Worst Pollution Problems 2016: The Toxics Beneath our Feet*; Pure Earth and Green Cross Switzerland: New York, NY, USA; Zurich, Switzerland, 2016; p. 29.
- Whitmee, S.; Haines, A.; Beyrer, C.; Boltz, F.; Capon, A.G.; de Dias, B.F.S.; Ezeh, A.; Frumkin, H.; Gong, P.; Head, P.; et al. Safeguarding human health in the Anthropocene epoch: Report of The Rockefeller Foundation–Lancet Commission on planetary health. *Lancet* **2015**, *386*, 1973–2028. [CrossRef]
- Prüss-Ustün, A.; Vickers, C.; Haefliger, P.; Bertollini, R. Knowns and unknowns on burden of disease due to chemicals: A systematic review. *Environ. Health* **2011**, *10*, 9. [CrossRef] [PubMed]
- Jiménez-Chillarón, J.C.; Nijland, M.J.; Ascensão, A.A.; Sardão, V.A.; Magalhães, J.; Hitchler, M.J.; Domann, F.E.; Oliveira, P.J. Back to the future: Transgenerational transmission of xenobiotic-induced epigenetic remodeling. *Epigenetics* **2015**, *10*, 259–273. [CrossRef]
- Nilsson, E.E.; Sadler-Riggelman, I.; Skinner, M.K. Environmentally induced epigenetic transgenerational inheritance of disease. *Environ. Epigenet.* **2018**, *4*, dvy016. [CrossRef]
- Stewart, A.G.; Hursthouse, A.S. Environment and Human Health: The Challenge of Uncertainty in Risk Assessment. *Geosciences* **2018**, *8*, 24. [CrossRef]
- WHO. *Childhood Lead Poisoning*; World Health Organisation: Geneva, Switzerland, 2010; ISBN 978-92-4-150033-3.
- Nevin, R. How lead exposure relates to temporal changes in IQ, violent crime, and unwed pregnancy. *Environ. Res.* **2000**, *83*, 1–22. [CrossRef]
- European Chemicals Agency. Understanding REACH. Available online: <https://echa.europa.eu/regulations/reach/understanding-reach> (accessed on 12 January 2020).
- Gallacher, J.; Bronsterng, K.; Palmer, S.; Fone, D.; Lyons, R. Symptomatology attributable to psychological exposure to a chemical incident: A natural experiment. *J. Epidemiol. Commun. Health* **2007**, *61*, 506–512. [CrossRef]
- Stewart, A.G.; Luria, P.; Reid, J.; Lyons, M.; Jarvis, R. Real or Illusory? Case Studies on the Public Perception of Environmental Health Risks in the North West of England. *Int. J. Environ. Res. Public Health* **2010**, *7*, 1153–1173. [CrossRef] [PubMed]
- Stewart, S.; Holland, W.W. *Screening in Disease Prevention: What Works*; Nuffield Trust: London, UK, 2005; pp. 1–16, ISBN 1-85775-770-X.

17. Wilson, J.M.G.; Jungner, G. *Principles and Practice of Screening for Disease*; Public Health Papers; World Health Organization: Geneva, Switzerland, 1968; p. 168.
18. Stange, B.; McInerney, J.; Golden, A.; Benade, W.; Neill, B.; Mayer, A.; Witter, R.; Tenney, L.; Stinson, K.; Cragle, D.; et al. Integrated approach to health screening of former department of energy workers detects both occupational and non-occupational illness. *Am. J. Ind. Med.* **2016**, *59*, 200–211. [[CrossRef](#)] [[PubMed](#)]
19. NHS Screening. Available online: <https://www.nhs.uk/conditions/nhs-screening/> (accessed on 24 August 2020).
20. Dobrow, M.J.; Hagens, V.; Chafe, R.; Sullivan, T.; Rabeneck, L. Consolidated principles for screening based on a systematic review and consensus process. *Can. Med. Assoc. J.* **2018**, *190*, E422–E429. [[CrossRef](#)] [[PubMed](#)]
21. Andermann, A.; Blancquaert, I.; Beauchamp, S.; Déry, V. Revisiting Wilson and Jungner in the genomic age: A review of screening criteria over the past 40 years. *Bull. World Health Organ.* **2008**, *86*, 317–319. [[CrossRef](#)]
22. Cragun, D.; DeBate, R.D.; Pal, T. Applying Public Health Screening Criteria: How Does Universal Newborn Screening Compare to Universal Tumor Screening for Lynch Syndrome in Adults with Colorectal Cancer? *J. Genet. Couns.* **2015**, *24*, 409–420. [[CrossRef](#)] [[PubMed](#)]
23. Pollitt, R.J. Principles and performance: Assessing the evidence. *Acta Paediatr.* **1999**, *88*, 110–114. [[CrossRef](#)] [[PubMed](#)]
24. Grosse, S.D.; Boyle, C.A.; Kenneson, A.; Khoury, M.J.; Wilfond, B.S. From Public Health Emergency to Public Health Service: The Implications of Evolving Criteria for Newborn Screening Panels. *Pediatrics* **2006**, *117*, 923–929. [[CrossRef](#)]
25. Lindegren, M.L.; Kobrynski, L.; Rasmussen, S.A.; Moore, C.A.; Grosse, S.D.; Vanderford, M.L.; Spira, T.J.; McDougal, J.S.; Vogt, R.F.; Hannon, W.H.; et al. Applying public health strategies to primary immunodeficiency diseases: A potential approach to genetic disorders. *MMWR Recomm. Rep.* **2004**, *53*, 1–29.
26. Harris, R.; Sawaya, G.F.; Moyer, V.A.; Calonge, N. Reconsidering the Criteria for Evaluating Proposed Screening Programs: Reflections From 4 Current and Former Members of the U.S. Preventive Services Task Force. *Epidemiol. Rev.* **2011**, *33*, 20–35. [[CrossRef](#)]
27. UK National Screening Committee. *First Report of the National Screening Committee*; Health Departments of the United Kingdom: London, UK, 1998; p. 45.
28. Mahoney, G.; Stewart, A.G.; Kennedy, N.; Whitely, B.; Turner, L.; Wilkinson, E. Achieving attainable outcomes from good science in an untidy world: Case studies in land and air pollution. *Environ. Geochem. Health* **2015**, *37*, 689–706. [[CrossRef](#)]
29. NHS Screening. Available online: http://www.nsc.nhs.uk/uk_nsc/uk_nsc_ind.htm (accessed on 1 August 2005).
30. Ghebrehewet, S.; Stewart, A.G.; Baxter, D.; Shears, P.; Conrad, D.; Kliner, M. (Eds.) *Health Protection: Principles and Practice*; OUP Oxford: Oxford, UK, 2016; ISBN 978-0-19-874547-1.
31. Hsiao, L.-L. Raising awareness, screening and prevention of chronic kidney disease: It takes more than a village. *Nephrology* **2018**, *23*, 107–111. [[CrossRef](#)]
32. Trasande, L.; Ziebold, C.; Schiff, J.S.; Wallinga, D.; McGovern, P.; Oberg, C.N. The role of the environment in pediatric practice in Minnesota: Attitudes, beliefs, and practices. *Minn. Med.* **2008**, *91*, 36–39. [[PubMed](#)]
33. Bernard, S.M. Should the Centers for Disease Control and Prevention’s Childhood Lead Poisoning Intervention Level Be Lowered? *Am. J. Public Health* **2003**, *93*, 1253–1260. [[CrossRef](#)]
34. Jackson, R.J.; Cummins, S.K.; Tips, N.M.; Rosenblum, L.S. Preventing Childhood Lead Poisoning: The Challenge of Change. *Am. J. Prev. Med.* **1998**, *14*, 84–86. [[CrossRef](#)]
35. Etchevers, A.; Glorennec, P.; Le Strat, Y.; Lecoffre, C.; Bretin, P.; Le Tertre, A. Screening for Elevated Blood Lead Levels in Children: Assessment of Criteria and a Proposal for New Ones in France. *Int. J. Environ. Res. Public Health* **2015**, *12*, 15366–15378. [[CrossRef](#)] [[PubMed](#)]
36. Neuwirth, L.S. Resurgent lead poisoning and renewed public attention towards environmental social justice issues: A review of current efforts and call to revitalize primary and secondary lead poisoning prevention for pregnant women, lactating mothers, and children within the U.S. *Int. J. Occup. Environ. Health* **2018**, *24*, 86–100. [[PubMed](#)]
37. Bruce, S.A.; Christensen, K.Y.; Coons, M.J.; Havlena, J.A.; Meiman, J.G.; Walsh, R.O. Using Medicaid Data to Improve Childhood Lead Poisoning Prevention Program Outcomes and Blood Lead Surveillance. *J. Public Health Manag. Pract.* **2019**, *25*, S51. [[CrossRef](#)] [[PubMed](#)]
38. Weitzman, M. Blood Lead Screening and the Ongoing Challenge of Preventing Children’s Exposure to Lead. *JAMA Pediatr.* **2019**, *173*, 517–519. [[CrossRef](#)] [[PubMed](#)]

39. Kaplowitz, S.A.; Perlstadt, H.; D’Onofrio, G.; Melnick, E.R.; Baum, C.R.; Kirrane, B.M.; Post, L.A. The Predictive Value of Self-Report Questions in a Clinical Decision Rule for Pediatric Lead Poisoning Screening. *Public Health Rep.* **2012**, *127*, 375–382. [[CrossRef](#)]
40. Rooney, B.L.; Allen, B.K.; Strutt, P.J.; Hayes, E.B. Development of a Screening Tool for Prediction of Children at Risk for Lead Exposure in a Midwestern Clinical Setting. *Pediatrics* **1994**, *93*, 183–187.
41. Tejada, D.M.; Wyatt, D.D.; Rostek, B.R.; Solomon, W.B. Do Questions About Lead Exposure Predict Elevated Lead Levels? *Pediatrics* **1994**, *93*, 192–194.
42. Burns, M.S.; Shah, L.H.; Marquez, E.R.; Denton, S.L.; Neyland, B.A.; Vereschagin, D.; Gremse, D.A.; Gerstenberger, S.L. Efforts to Identify At-Risk Children for Blood Lead Screening in Pediatric Clinics—Clark County, Nevada. *Clin. Pediatr.* **2012**, *51*, 1048–1055. [[CrossRef](#)] [[PubMed](#)]
43. Grindler, N.M.; Allshouse, A.A.; Jungheim, E.; Powell, T.L.; Jansson, T.; Polotsky, A.J. OBGYN screening for environmental exposures: A call for action. *PLoS ONE* **2018**, *13*, e0195375. [[CrossRef](#)] [[PubMed](#)]
44. Thompson, N.J.; Youngman, M.J.; Moody, J.; McColl, N.P.; Cos, D.R.; Astbury, J.; Webb, S.; Prosser, S.L. *Radiation Monitoring Units: Planning and Operational Guidance*; Health Protection Agency, Centre for Radiation, Chemicals and Environmental Hazards: Chilton, UK, 2011; p. 98.
45. Rojas-Palma, C.; Liland, A.; Jerstad, A.N.; Etherington, G.; del Rosario Perez, M.; Rahola, T.; Smith, K. (Eds.) *TMT Handbook. Triage, Monitoring and Treatment of People Exposed to Ionising Radiation Following a Malevolent Act*; NRPA: Østerås, Norway, 2009; ISBN 978-82-90362-27-5.
46. Kotaki, K.; Ikeda, H.; Fukuda, T.; Yuki, F.; Hasuo, K.; Kawano, Y.; Kawasaki, M. Effectiveness of diagnostic screening tests in mass screening for COPD using a cooperative regional system in a region with heavy air pollution: A cross-sectional study. *BMJ Open* **2017**, *7*, e012923. [[CrossRef](#)] [[PubMed](#)]
47. Vearrier, D.; Greenberg, M.I. The implementation of medical monitoring programs following potentially hazardous exposures: A medico-legal perspective. *Clin. Toxicol.* **2017**, *55*, 956–969. [[CrossRef](#)]
48. Gaskin, J.; Rennie, C.; Coyle, D. Reducing Periconceptional Methylmercury Exposure: Cost–Utility Analysis for a Proposed Screening Program for Women Planning a Pregnancy in Ontario, Canada. *Environ. Health Perspect.* **2015**, *123*, 1337–1344. [[CrossRef](#)]
49. Garty, G.; Karam, P.A.; Brenner, D.J. Infrastructure to Support Ultra High Throughput Biodosimetry Screening after a Radiological Event. *Int. J. Radiat. Biol.* **2011**, *87*, 754–765. [[CrossRef](#)]
50. Vaidyanathan, A.; Staley, F.; Shire, J.; Muthukumar, S.; Kennedy, C.; Meyer, P.A.; Brown, M.J. Screening for Lead Poisoning: A Geospatial Approach to Determine Testing of Children in At-Risk Neighborhoods. *J. Pediatr.* **2009**, *154*, 409–414. [[CrossRef](#)]
51. Nieder, A.M.; MacKinnon, J.A.; Fleming, L.E.; Kearney, G.; Hu, J.J.; Sherman Recinda, L.; Huang, Y.; Lee David, J. Bladder Cancer Clusters in Florida: Identifying Populations at Risk. *J. Urol.* **2009**, *182*, 46–51. [[CrossRef](#)]
52. Emery, R.J.; Sprau, D.D.; Morecook, R.C. Risk communication considerations to facilitate the screening of mass populations for potential contamination with radioactive material. *Health Phys.* **2008**, *95*, S168–S174. [[CrossRef](#)]
53. Kardamanidis, K.; Lyle, D.M.; Boreland, F. Addressing decreasing blood lead screening rates in young children in Broken Hill, NSW. *NSW Public Health Bull.* **2008**, *19*, 180–182. [[CrossRef](#)] [[PubMed](#)]
54. Hays, S.M.; Becker, R.A.; Leung, H.W.; Aylward, L.L.; Pyatt, D.W. Biomonitoring equivalents: A screening approach for interpreting biomonitoring results from a public health risk perspective. *Regul. Toxicol. Pharmacol.* **2007**, *47*, 96–109. [[CrossRef](#)] [[PubMed](#)]
55. Glorennec, P.; Declercq, C. Performance of several decision support tools for determining the need for systematic screening of childhood lead poisoning around industrial sites. *Eur J. Public Health* **2007**, *17*, 47–52. [[CrossRef](#)] [[PubMed](#)]
56. Holisaz, M.T.; Rayegani, S.M.; Hafezy, R.; Khedmat, H.; Motamedi, M.H.K. Screening for peripheral neuropathy in chemical warfare victims. *Int. J. Rehabil. Res.* **2007**, *30*, 71–74. [[CrossRef](#)]
57. Howell, E.M.; Russette, L. An innovative blood lead screening program for Indian children. *Public Health Rep.* **2004**, *119*, 141–143. [[CrossRef](#)]
58. Dignam, T.A.; Evens, A.; Eduardo, E.; Ramirez, S.M.; Caldwell, K.L.; Kilpatrick, N.; Noonan, G.P.; Flanders, W.D.; Meyer, P.A.; McGeehin, M.A. High-Intensity Targeted Screening for Elevated Blood Lead Levels Among Children in 2 Inner-City Chicago Communities. *Am. J. Public Health* **2004**, *94*, 1945–1951. [[CrossRef](#)]

59. Grivas, T.B.; Samelis, P.; Polyzois, B.D.; Giourelis, B.; Polyzois, D. School screening in the heavily industrialized area—Is there any role of industrial environmental factors in idiopathic scoliosis prevalence? *Stud. Health Technol. Inform.* **2002**, *91*, 76–80.
60. Kitamura, K.; Yoshikawa, K.; Iwama, M.; Nagao, M. Justification of measurement of eight congeners levels instead of twenty congeners of dioxins for mass screening of human exposure. *J. Toxicol. Sci.* **2001**, *26*, 163–168. [[CrossRef](#)]
61. Karp, R.; Abramson, J.; Clark-Golden, M.; Mehta, S.; Daniele, R.M.; Homel, P.; Deutsch, J. Should we screen for lead poisoning after 36 months of age? Experience in the inner city. *Ambul. Pediatr.* **2001**, *1*, 256–258. [[CrossRef](#)]
62. Rolnick, S.J.; Nordin, J.; Cherney, L.M. A comparison of costs of universal versus targeted lead screening for young children. *Environ. Res.* **1999**, *80*, 84–91. [[CrossRef](#)]
63. Fletcher, A.M.; Gelberg, K.H.; Marshall, E.G. Reasons for Testing and Exposure Sources Among Women of Childbearing Age with Moderate Blood Lead Levels. *J. Commun. Health* **1999**, *24*, 215–227. [[CrossRef](#)] [[PubMed](#)]
64. Parsons, P.J.; Reilly, A.A.; Esernio-Jenssen, D. Screening children exposed to lead: An assessment of the capillary blood lead fingerstick test. *Clin. Chem.* **1997**, *43*, 302–311. [[CrossRef](#)] [[PubMed](#)]
65. Binder, S.; Matte, T.D.; Kresnow, M.; Houston, B.; Sacks, J.J. Lead testing of children and homes: Results of a national telephone survey. *Public Health Rep.* **1996**, *111*, 342–346. [[PubMed](#)]
66. Wallace, R.B.; Murray, R.F. Workshop 1: High-risk populations—screening and prevention research strategies. *Prevent. Med.* **1994**, *23*, 569–570. [[CrossRef](#)] [[PubMed](#)]
67. Carpenter, J.W. Pediatric lead level screening. *Alaska Med.* **1993**, *35*, 173.
68. Wartenberg, D. Screening for lead exposure using a geographic information system. *Environ. Res.* **1992**, *59*, 310–317. [[CrossRef](#)]
69. Webb, K.B. The pilot Missouri health effect study. *Bull. Environ. Contam. Toxicol.* **1984**, *33*, 662–672. [[CrossRef](#)]
70. Shigematsu, I.; Minowa, M.; Yoshida, T.; Miyamoto, K. Recent results of health examinations on the general population in cadmium-polluted and control areas in Japan. *Environ. Health Perspect.* **1979**, *28*, 205–210. [[CrossRef](#)]
71. Hursthouse, A.; Kowalczyk, G. Transport and dynamics of toxic pollutants in the natural environment and their effect on human health: Research gaps and challenge. *Environ. Geochem. Health* **2009**, *31*, 165–187. [[CrossRef](#)]
72. Bommarito, P.A.; Beck, R.; Douillet, C.; Razo, L.M.D.; Garcia-Vargas, G.-G.; Valenzuela, O.L.; Sanchez-Peña, L.C.; Styblo, M.; Fry, R.C. Evaluation of plasma arsenicals as potential biomarkers of exposure to inorganic arsenic. *J. Expo. Sci. Environ. Epidemiol.* **2019**, *29*, 718–729. [[CrossRef](#)]
73. Public Health England Evidence Review Criteria: National Screening Programmes. Available online: <https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes> (accessed on 20 May 2020).
74. Gray, J.A.M.; Patnick, J.; Blanks, R.G. Maximising benefit and minimising harm of screening. *BMJ* **2008**, *336*, 480–483. [[CrossRef](#)] [[PubMed](#)]
75. Swaine, Z. Medical Model. In *Encyclopedia of Clinical Neuropsychology*; Kreutzer, J.S., DeLuca, J., Caplan, B., Eds.; Springer: New York, NY, USA, 2011; pp. 1542–1543, ISBN 978-0-387-79948-3.
76. Hosseini Shokouh, S.M.; Arab, M.; Emamgholipour, S.; Rashidian, A.; Montazeri, A.; Zaboli, R. Conceptual Models of Social Determinants of Health: A Narrative Review. *Iran. J. Public Health* **2017**, *46*, 435–446. [[PubMed](#)]
77. Galama, T.J.; van Kippersluis, H. A Theory of Socio-economic Disparities in Health over the Life Cycle. *Econ. J.* **2019**, *129*, 338–374. [[CrossRef](#)] [[PubMed](#)]
78. CDC. The Social-Ecological Model: A Framework for Prevention. Available online: <https://www.cdc.gov/violenceprevention/publichealthissue/social-ecologicalmodel.html> (accessed on 18 August 2020).
79. Olvera Alvarez, H.A.; Appleton, A.A.; Fuller, C.H.; Belcourt, A.; Kubzansky, L.D. An Integrated Socio-Environmental Model of Health and Well-Being: A Conceptual Framework Exploring the Joint Contribution of Environmental and Social Exposures to Health and Disease Over the Life Span. *Curr. Environ. Health Rep.* **2018**, *5*, 233–243. [[CrossRef](#)] [[PubMed](#)]

80. Vandenberg, L.N.; Colborn, T.; Hayes, T.B.; Heindel, J.J.; Jacobs, D.R., Jr.; Lee, D.-H.; Shioda, T.; Soto, A.M.; vom Saal, F.S.; Welshons, W.V.; et al. Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. *Endocr. Rev.* **2012**, *33*, 378–455. [[CrossRef](#)] [[PubMed](#)]
81. Stewart, A.G.; Carter, J. Towards the development of a multidisciplinary understanding of the effects of toxic chemical mixtures on health. *Environ. Geochem. Health* **2009**, *31*, 239–251. [[CrossRef](#)]
82. Hernández, A.F.; Gil, F.; Tsatsakis, A.M. Chapter 33—Biomarkers of Chemical Mixture Toxicity. In *Biomarkers in Toxicology*, 2nd ed.; Gupta, R.C., Ed.; Academic Press: Cambridge, MA, USA, 2019; pp. 569–585, ISBN 978-0-12-814655-2.
83. Ross, L.F. Screening for conditions that do not meet the Wilson and Jungner criteria: The case of Duchenne muscular dystrophy. *Am. J. Med. Genet. Part. A* **2006**, *140*, 914–922. [[CrossRef](#)]
84. Pienaar, K.; Petersen, A.; Bowman, D.M. Matters of fact and politics: Generating expectations of cancer screening. *Soc. Sci. Med.* **2019**, *232*, 408–416. [[CrossRef](#)]
85. Gray, J.A.M. Evidence based policy making. *BMJ* **2004**, *329*, 988–989. [[CrossRef](#)]
86. Petros, M. Revisiting the Wilson-Jungner criteria: How can supplemental criteria guide public health in the era of genetic screening? *Genet. Med.* **2012**, *14*, 129–134. [[CrossRef](#)]

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).