The Noise/Stress Concept, Risk Assessment and Research Needs

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In principle, the noise/stress hypothesis is well understood: Noise activates the pituitary-adrenal-cortical axis and the sympathetic-adrenal-medullary axis. Changes in stress hormones including epinephrine, norepinephrine and cortisol are frequently found in acute and chronic noise experiments. The catecholamines and steroid hormones affect the organism's metabolism. Cardiovascular disorders are especially in focus for epidemiological studies on adverse noise effects. However, not all biologically notifiable effects are of clinical relevance. The relative importance and significance of health outcomes to be assessed in epidemiological noise studies follow a hierarchical order, i.e. changes in physiological stress indicators, increase in biological risk factors, increase of the prevalence or incidence of diseases, premature death. Decision-making and risk management rely on quantitative risk assessment. Epidemiological methods are the primary tool for providing the necessary information. However, the statistical evidence of findings from individual studies is often weak. Magnitude of effect, dose-response relationship, biological plausibility and consistency of findings among studies are issues of epidemiological reasoning. Noise policy largely depends on considerations about cost-effectiveness, which may vary between populations. Limit or guideline values have to be set within the range between social and physical well-being - between nuisance and health. The cardiovascular risk is a key-outcome in non-auditory noise effects' research because of the high prevalence of related diseases in our communities. Specific studies regarding critical groups, different noise-sources, day/evening/night comparisons, coping styles and other effect-modifying factors, and the role of annoyance as a mediator of effect are issues for future research in this field.

Keywords: Risk assessment, Community noise, Health effects, Cardiovascular risk, Research needs, Reaction model, Epidemiology

Why study cardiovascular health effects of noise?

It is common experience that noise is unpleasant. It disturbs and interferes with activities of the individual, and most people do not want it (Miedema H.M.E. and Vos H., 1998; WHO European Centre for Environment and Health, 1995). Would it not be sufficient, from this point of view, to refer to social surveys when making decisions? Furthermore, annoyance-related noise standards are usually lower than (physical) health related standards. (Here and in the following the term “health” is used in the somatic meaning of the WHO definition, referring to physical health (WHO, 1948; WHO Regional Office for Europe, 1990).)

The answer is no! Decision makers have to make their decisions on rational grounds of limited resources, concurring risks and quality targets. They strongly rely on cost-effectiveness and cost-benefit considerations (Brown S., 1985; Cleland-Hamnett W., 1993; Moghissi A. A., 1993). The setting of environmental standards including limit values, guideline values and other standards is not a purely scientific task in this respect. This was pointed out by Rohrmann (Rohrmann B., 1993): “Critical limits for environmental stressors cannot be derived from empirical sciences. They are socio-political settings that depend on the weighing system of

all groups involved. Limit values are a normative act as a result of complex considerations about benefits, risks and costs" (translated from German into English).

With regard to noise, decisions have to be made within the spectrum of evaluation criteria between "comfort" (of quietness) and (physical) health" or one may say "nuisance and disease" (Babisch W., 2000a; Lindström B., 1992). Whereas quality targets at the lower end of this scale may be much more flexible, quality targets at the upper end reflect "the most tolerable exposure" and should be more obliging for ethical reasons. For example, environmental noise standards often refer to the area where people live as purely residential, commercial or mixed. From the equality point of view, it seems to be difficult to understand that health-related standards are different for different groups of people. On the other hand, regarding nuisance it is not a problem to accept different limit values.

Noise effects research on stress-related and cardiovascular outcomes provides the necessary information to identify thresholds for an increase in health risk, and to define the highest tolerable noise levels.

This direction is clearly stated in section 1, chapter 6 of the Agenda 21 – the global action plan of the United Nations' conference held in Rio de Janeiro in 1992 (UN, 1993). There, five health-related target areas were addressed, of which three could be directly applied to community noise. These are: the reduction of health risks related to the environment, the health problems in cities, and the protection of sensitive groups (Schwenk M., 2000). The emphasis here is on health risk. Furthermore, it was stated explicitly in the protocol, that "nationally determined action programmes, with international assistance, support and coordination, where necessary, in this area should include: development of criteria for maximum permitted safe noise exposure levels, and promote noise assessment and control as part of environmental health programmes". Transportation noise was addressed as a major factor of concern in this respect at the 3rd European Ministerial Conference held in London in 1999 (WHO, 1999).

Risk evaluation process

A conceptual framework for the regulation of environmental hazards was given by the US National Research Council (National Research Council, 1983; Patton D. E., 1993). It is illustrated in Figure 1 (adopted from (Neus H. and Biokat U., 2000)). The process of risk assessment (risk evaluation) comprises hazard identification ("Which health outcome is

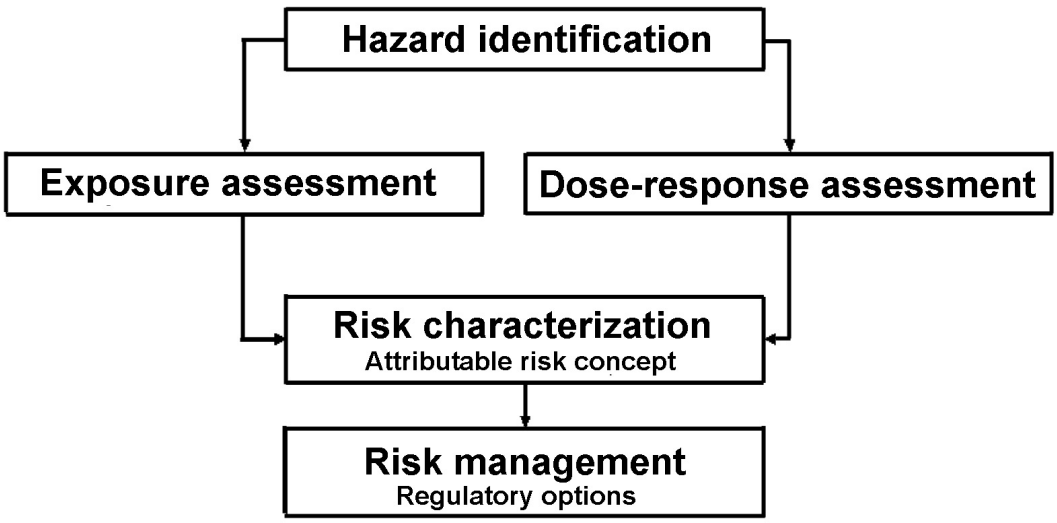

Figure 1. Process of risk evaluation

relevant?"), exposure assessment ("How many are affected") and dose-response assessment ("Threshold of effect"). This information is summarized in, what is called, "risk characterization" ("health hazard characterization"). It involves the interpretation of the available evidence from the available data and other scientific disciplines, and is subject to the discussion of uncertainties including chance, bias and validity of studies as well as transparency, replicability and comprehensiveness of reviews. As a result of the risk evaluation process, a quantitative estimate about the likelihood that the hazard will affect exposed people will be derived. Usually attributable risk percentages will be calculated (Walter S. D., 1998). This will serve as key information for any kind of risk management including regulatory options (Jasanoff S., 1993).

The noise issue was recently discussed by Neus and Boikat in this context (Neus H. and Biokat U., 2000). Further details about the risk evaluation process are given elsewhere (WHO Regional Office for Europe, 2000). The term "risk" in this context is not synonymous with "danger" (Fülgraff G., 1992; Zeger S. L., 1991). "Risk" is the numerical quantification of danger. That is the statistical likelihood for a certain damage to occur within a period of time or as a result of a distinct event. Dealing with risks includes the acceptance of a risk, which is a dynamic process depending on changing knowledge, attitudes, views, technical development and costs. For example, according to WHO guidelines for drinking water, the tolerable lifetime risk of death due to cancer is 1:100,000 (Scheuplein R. J., 1993; WHO, 1993). This value reflects a socially accepted background risk (Dieter H. H. and Grohmann A., 1995).

Adverse health effect

The severity of the health outcome, it's prevalence in the general population, the frequency of exposure considered relevant for health, and the magnitude of effect are important issues in risk impact assessment (Neus H. and Biokat U., 2000). The term "adverse" is essential in this context of environmental standard setting. Risk management should ensure that "adverse" health effects cannot occur. Decisions on whether or not any effect is adverse, requires expert judgement. The World Health Organization defines an "adverse effect" as follows (WHO, 1994): "Change in morphology, physiology, growth, development or life span of an organism, which results in impairment of the functional capacity to compensate for additional stress, or increase in susceptibility to the harmful effect of other environmental influences". It is obvious that the relevance of a noise effect increases with increasing severity and the high prevalence of the considered health outcome. Ischemic heart diseases are one of the major causes of premature death in modern societies (Doll R., 1992; WHO Regional Office Europe, 1999). For this reason cardiovascular disorders including hypertension and myocardial infarction have been in the primary focus of epidemiological noise research.

Figure. 2 is adapted from Wichmann (Wichmann H. E., 1992). It originally refers to chemical exposures, and summarizes the types of possible responses of the organism towards an environmental agent. However, in more general terms, it can be applied to any kind of exposure or environmental factor. The term "internal exposure" at the bottom of the triangle of Figure. 2 is not relevant for noise. In contradiction to such environmental factors like lead, cadmium or benzene, noise is not an exogenous factor that accumulates in the organism. One cannot measure "noise" in the organism, only its effects. However, "internal exposure" may be substituted with "annoyance" here as a "soft" outcome. Next in the triangle comes "physiological changes of unknown significance" followed by "pathological changes", "morbidity" and "mortality" or "life span". Effects regarding the top three outcomes of the triangle may be attributed "adverse" according to the WHO criteria.

The fact that an organism responds to noise does not have to be per se "adverse". In noise research, we are looking at endogeneous response variables that are physiological components/substances within the organism, and

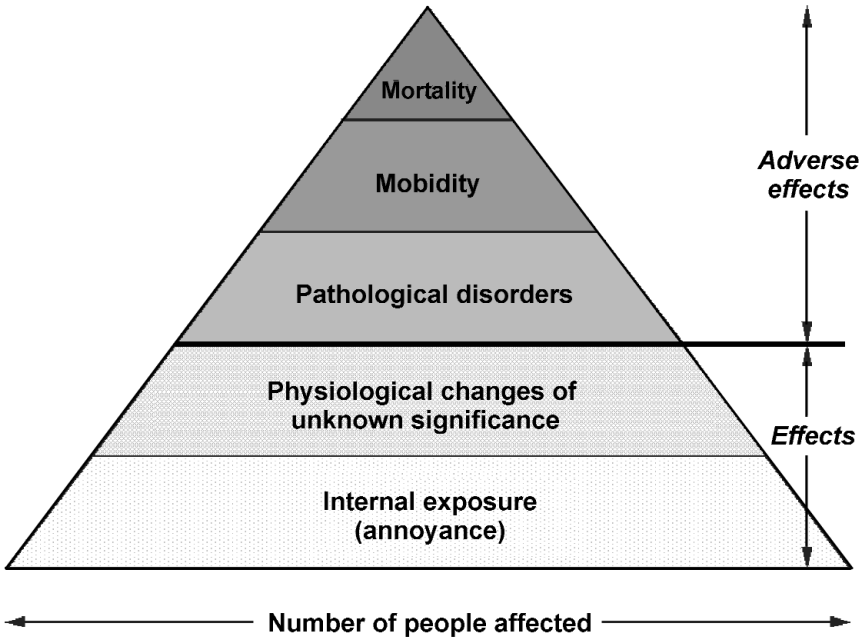

Figure 2. Severity of (noise) effects

which are related to the natural stress mechanism. For example, thresholds of acute changes in EEG, finger pulse amplitude, stress hormones - the whole startle reaction - may be interpreted in terms of no/lowest observed effect levels, using the terminology used in toxicological science (NOEL and LOEL) (Dieter H. H., 1995). However, they may not have pathological significance. Furthermore, due to improvements of measuring techniques, thresholds tend to decline to levels without clinical relevance. Therefore, NOEL and LOEL may not be suitable for decision making in general.

It is sometimes suggested to refer to exceedances of “normal values” of physiological factors as a criterion of effect. However, even such exceedances are not necessarily associated with an increased risk. Physiological normal values are often simply defined from statistical grounds of distributions. However, once there is quantitative evidence that subjects with a chronically high biological value above normal run a higher risk for subsequent disorders, then we call this factor a risk factor per definition, and it is of clinical relevance. In such cases, we are looking at no/lowest observed adverse effect levels (NOAEL and LOAEL), which indeed may have implication for noise policy according to the WHO recommendations. They are commonly used in public health policy for preventive action. In order to obtain reasonably safe standards, it is usual to start from the NOAEL and to apply additional safety or uncertainty factors (Arnold et al., 1997; Neus H. and Biokat U., 2000; WHO, 1994).

Reaction Schema

Much research has been carried out in the laboratory validating the principle reaction model. The essentials are this:

- Sound/noise is a psychosocial stressor that activates the sympathetic and endocrine system.

- Acute noise effects do not only occur at high sound levels in occupational settings, but also at relatively low environmental sound levels when, more importantly, certain activities such as concentration, relaxation or sleep are disturbed.

Epidemiology plays a unique role in the assessment of health risk from environmental factors and the determination of NOAELs and LOAELs (Samet J. M. *et al.*, 1998). Unlike

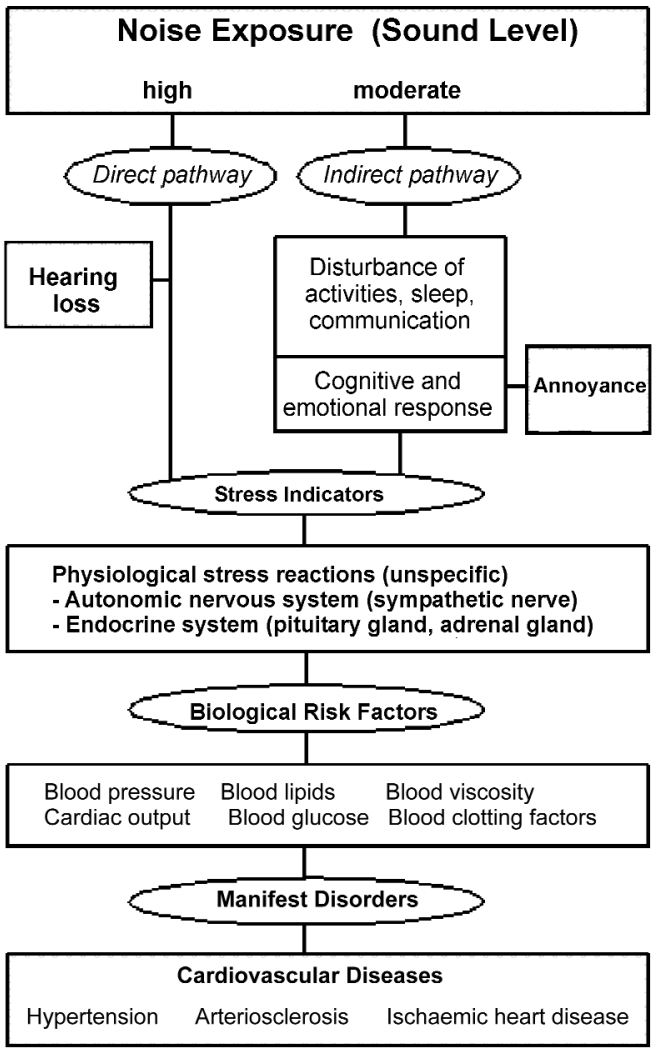

Figure 3. Noise effects reaction schema

laboratory experiments, it provides a most straightforward way of health impact assessment on evidence-based information about the exposure-response function obtained under "true life conditions" (Babisch W. *et al.*, 1992; Pearce N., 1999). It largely avoids the extrapolations across species and levels of exposure (WHO Regional Office for Europe, 2000), and is an essential component for the effective practice of public health policy (Adami H.-O. and Trichopoulos D., 1999; Hertz-Picciotto I., 1995; Savitz D.A. *et al.*, 1999; Soskolne L. C., 1999).

This reaction scheme which is given in Figure. 3 can be used for hypothesis testing in noise epidemiology considering the cause-effect chain i.e.: sound - annoyance (noise) - physiological arousal (stress indicators) - (biological) risk factors - disease - and mortality (the latter is not explicitly considered in the graph).

The mechanism works either directly through the synaptic nervous interactions in the reticular activating system and parts of the between-brain (including the hypothalamus), or indirectly through the emotional and the cognitive perception of the sound via the cortical and sub-cortical structures including the lymbic region (Andersson K. and Lindvall T., 1988; Spreng M., 2000). According to the general stress model, neuroendocrine arousal affects the humoral and metabolic state of the organism, and acts as a mediator along the pathway from the perceived sound to the stress-related disease (Henry J. P., 1992). In principle, a variety of well-known and established risk factors may be affected. Many are well recognized as risk factors for ischemic heart disease such as blood lipids, glucose level, haemodynamic and haemostatic factors.

As outlined in Figure. 3, there are three levels of physiological outcome, which are of interest in epidemiological noise research on cardiovascular effects. These are: stress indicators (e.g. stress hormones), risk factors (e. g. blood pressure, blood lipids, haemostatic factors), and manifest diseases (e. g. hypertension, ischaemic heart disease) (Babisch W., 2000a; Babisch W. *et al.*, 2001).

- Noise effects on stress indicators have no direct clinical relevance in terms of health. Stress indicators, however, are particularly useful for investigating biological mechanisms because they are short-term reacting parameters, which occur at the beginning of the reaction chain.

- Noise effects on established biological risk factors have a direct relevance to health (per definition). Even small non-pathological changes of mean values in population may be of clinical relevance. But, for a quantitative risk assessment, external sources of data would have to be used. (E.g., what does an "x%" increase in cholesterol level in an exposed group mean with regard to the risk of myocardial infarction?)

- Noise effects with regard to the prevalence or incidence of manifest diseases as a statistical endpoints clearly have a relevance to health. From the collected data it is possible to carry out a directly quantitative risk assessment. However, since distinct rare events are the basis, large study samples are needed for achieving statistically significant results.

Cardiovascular risk

The body of literature of epidemiological studies on the relationship between community noise and cardiovascular health appears to be small compared to other environmental disciplines. Furthermore, studies often suffer from exposure misclassification, low statistical power, insufficient control of confounding, and the lack of dose-response design. Even if one accepts the hypothesis of a qualitative association between noise and cardiovascular risk, it is difficult to interpret study results with regard to thresholds of effect.

In the recent years some review articles have been published (Babisch W., 2000b; Berglund B. and Lindvall T., 1995; Gezondheitsraad, 1994; Gezondheitsraad, 1999; IEH, 1997; Passchier-Vermeer W. and Passchier W. F., 2000; Porter N. D. *et al.*, 1998) trying to assess the evidence of the relationship between community noise and cardiovascular disease outcomes. These criteria are often based on recommendations given by the International Agency for Research on Cancer (IARC, 1987):

Sufficient evidence is given if a positive relationship is observed between exposure to the agent and the health outcome (cancer), in studies in which chance, bias and confounding can be ruled out with reasonable confidence.

Limited evidence is given if a positive association is observed between exposure to the agent and the health outcome (cancer), for which a causal interpretation is considered by a Working Group (experts) to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.

Inadequate evidence is given if the available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association.

The distinction among the categories is chiefly based on reproducibility of the evidence between studies, the validity (absence of bias and confounding), and the role of chance. Causality in epidemiology can never be completely proven (Christoffel T. and Teret S. P., 1991; Schlesselman J. J., 1987). It is a gradual term of which evidence is increasing with increasing number of facts. However, the magnitude of effect, presence of dose-response relationship, consistency with other studies in different populations and with different methodology, and coherence (biological plausibility) are commonly accepted arguments for a causal relationship (Bradford Hill A. Sir, 1965; Evans A. S., 1976; Morabia A., 1991; Weed D.L. and Hursting S.D., 1998).

The following ratings regarding the evidence of an effect of community noise on cardiovascular health were given from different experts and expert groups:

Health Council of the Netherlands, 1994 (Gezondheitsraad, 1994) and Passchier-Vermeer and Passchier, 2000 (Passchier-Vermeer W. and Passchier W. F., 2000)

"Limited" evidence for the relationship between noise (including occupational noise) and biochemical effects.

"Sufficient evidence for the relationship between noise (including occupational noise) and hypertension.

"Sufficient" evidence for a relationship between noise and ischaemic heart disease.

Institute for Environment and Health, 1997 (IEH, 1997) and Porter et al.,1998 (Porter N. D. *et al.*, 1998)

"Inconclusive" evidence for a causal link between noise exposure and hypertension.

"Sufficient" evidence for a causal association between noise exposure and ischaemic heart disease.

Health Council of the Netherlands, 1999 (Gezondheitsraad, 1999)

"Limited" evidence for the relationship between noise (including occupational noise) and biochemical effects.

"Sufficient" evidence for an association between ambient noise and hypertension.

"Sufficient" evidence for an association between ambient noise and ischaemic heart disease (observation threshold: $L_{eq,6\text{-}22\ h}$: 70 dB(A)).

Babisch, 2000 (Babisch W., 2000b)

"No" scientific evidence for association between transportation noise and mean blood pressure readings (exception: in children consistently higher readings were found in the exposed groups).

"Little" evidence regarding the association between transportation noise and hypertension.

"Some" evidence regarding the association between transportation noise and ischaemic heart disease. The latter was viewed as being "sufficient" for action.

Neus and Boikat, 2000 (Neus H. and Biokat U., 2000)

"Limited" evidence regarding the association between traffic noise and ischaemic heart disease.

In summarizing these statements, the status of evidence as concluded in the literature may be characterized as follows: biochemical effects – limited evidence, hypertension – inadequate/limited evidence, ischaemic heart disease – limited/sufficient.

Precautionary principle

We have to learn to live with uncertainties (Rose G., 1992; Scheuplein R. J., 1993). However, "no scientific evidence" does not mean "no effect" (Morrell S. *et al.*, 1997). The precautionary principle can be the ground on which decisions can be made, given the small and weak database that we at the moment have to rely on (WHO Regional Office for Europe, 2000). Horton stated the precautionary principle as:

"We must act on facts, and on the most accurate interpretation of them, using the best scientific information. That does not mean that we must sit back until we have 100% evidence about everything. Where the state of the health of the people is at stake, the risks can be so high and the costs of corrective action so great, that prevention is better than cure. We must analyse the possible benefits and costs of interaction. Where there are significant risks of damage to the public health, we should be prepared to take action to diminish those risks, even when the scientific knowledge is not conclusive, if the balance of likely costs and benefits justifies it." (Horton R., 1998).

From the few epidemiological studies that provide dose-response relationships between traffic noise and cardiovascular diseases it was estimated that the risk increases for values between 65 and 70 dB(A) of the daytime average A-weighted sound pressure level (Babisch W. *et al.*, 1992; Babisch W. *et al.*, 1993). 65 dB(A)

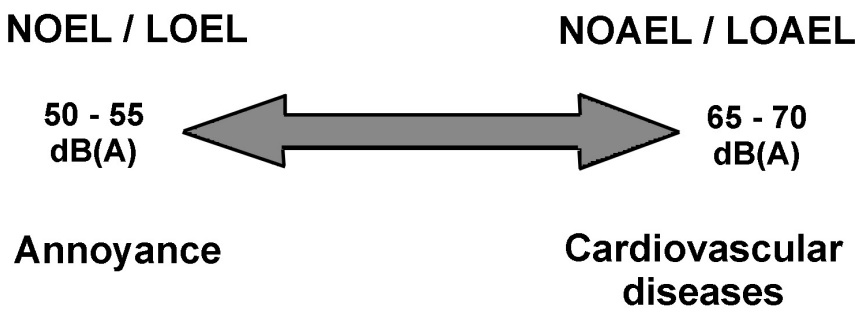

Figure 4. Evaluation spectrum: thresholds of noise effects ($L_{AFm,\ 6\text{-}22\ h}$)

may be viewed as a NOAEL in this context, and 70 dB(A) as a LOAEL for the present. At the lower end of the "nuisance-health scale", 55 dB(A) during daytime and evening (45 dB(A) during night-time, 30 dB(A) indoors during night-time) is the threshold and recommended value for ambient noise levels outdoors, to avoid serious annoyance (Europe WHO Regional Office, 2000; WHO, 2000). This is illustrated in Figure. 4.

Research needs

From laboratory-studies much information about biological mechanisms of the effects of noise have been derived. Questions that need to be answered are these: Do these changes observed in the laboratory habituate or do they persist under chronic noise exposure? If they habituate, what are the physiological costs? If they persist, what are the long-term health effects? Future epidemiological noise research will have to concentrate on the following questions:

- Who are sensitive or vulnerable groups of people (risk groups), for whom noise standards have to be adjusted for prevention? In practical terms, are factors such as: subjective noise sensitivity, negative affectivity, illness, gender, age, type A-behaviour, pregnancy and family history, effect modifiers on the relationship between noise and the health outcome of interest?

- Which hours of the day deserve special attention regarding the physiological response? In particular, sleep disturbances are of interest here, but also the recreational part of the day in the evening may be of particular interest.

- What are effective individual coping styles (mechanisms) that may reduce noise-induced stress reactions and health disorders?

- Are there source-specific differences in risk characterization? For example, are the associations between exposure and health outcome different for road, rail, and aircraft noise, similar to those known from studies on annoyance? Most of the epidemiological data refer to road traffic. Regarding aircraft noise hardly any dose-response curves are known. Nearly no epidemiological data is available regarding rail traffic.

- What are the appropriate indicators of exposure (regarding different noise sources)? For example: Leq, Lmax, number of events, frequency spectrum, particularly with regard to low frequency components.

- Do multiple exposures including non-noise stressors act additively, multiplicatively or synergistic on the outcome?

- How do objective (sound level) and subjective exposure (annoyance) interact regarding the relationship between noise and health outcomes?

Cardiovascular effects of noise play an important role in noise policy and decision-making. Particular emphasis should be placed on epidemiological research in the explicit assessment of no-effect thresholds of exposure

for the determination of NOAEL and LOAEL. This calls for the assessment of dose-response relationships. The better determined the shape of the exposure-response-curve the more reliable is the health impact assessment.

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