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Comparative risk and impact assessment for occupational and environmental health

Valutazione comparata del rischio e dell'impatto in medicina professionale ed ambientale

Jung-Der Wang
Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University and Department of Internal Medicine and Department of Environmental and Occupational Medicine, National Taiwan University Hospital, Taipei, Taiwan

Summary

In the quantification of burdens of diseases, QALY (quality-adjusted life year) or DALY (disability-adjusted life year) have been used for comparative assessment of population health. By adjusting the survival function with the mean of quality of life (QOL) at every time point *t* and summing up yearly throughout lifetime, we obtained the quality-adjusted life expectancy (QALE) with the unit of QALY:

$$\text{QALE} = \int E[Qol(t \mid x_i)]S(t \mid x_i)dt$$

Three environmental health issues were empirically assessed as examples: the contamination of underground water by chlorinated hydrocarbons from an electronics factory; the enforcement of helmet law in Taipei city; and occupational policies for protection of offspring of female lead workers. The likelihoods and expected numbers of new cases with liver cancer, head injury, or mentally impaired offspring born to mothers of lead workers were estimated, and these were then multiplied by the quality-adjusted life expectancy lost per case. The results showed that the ground water pollution produced a potential loss of 78

Riassunto

Per quantificare le conseguenze delle malattie, sono stati usati i QALY (*quality-adjusted life years* = anni di vita aggiustati per qualità) o i DALY (*disability-adjusted life years* = anni di vita aggiustati per invalidità), per una valutazione comparata della salute della popolazione. Aggiustando la funzione sopravvivenza con la media della qualità di vita in ogni momento *t* e sommandola anno per anno per tutta la vita, abbiamo ottenuto l'aspettativa di vita aggiustata per qualità (*quality-adjusted life expectancy* = QALE) con l'unità di QALY.

$$\text{QALE} = \int E[Qol(t \mid x_i)]S(t \mid x_i)dt$$

Tre temi di salute ambientale sono stati valutati empiricamente come esempi: la contaminazione delle acque sotterranee da parte di idrocarburi clorati proveniente da un'industria elettronica; l'utilità della legge sul casco nella città di Taipei; e gli orientamenti di medicina del lavoro per la protezione della prole delle lavoratrici del piombo. Sono stati stimati la probabilità ed il numero atteso di nuovi casi di cancro epatico, di danno cerebrale, e di figli di lavoratrici del piombo con disturbi mentali, che sono stati poi moltiplicati per l'aspet-

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Address/Indirizzo: Dr. Jung-Der Wang, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University, College of Public Health, Room 719, No. 17, Xu-Zhou Road, Taipei, Taiwan - Tel. +886/2/33228080 - Fax +886/2/23224660 - E-mail: jdwang@ntu.edu.tw

QALM (quality-adjusted life month) for the 1000 people in the downstream community. The enforcement of helmet law in Taipei would save 6240 QALY annually. The expected utility loss of the babies born to female lead workers was about 216 QALY. If the QOL was measured by psychometry, it could be applied in clinical outcome evaluation. If it was extended to consider the cost of illness, the financial burden to the National Health Insurance could be estimated. We conclude that this is a feasible method for comparative health risk/impact assessment for public health and clinical policy decisions. Eur. J. Oncol., 13 (1), 33-39, 2008

Key words: **quality of life (QOL), quality-adjusted life year (QALY), disability-adjusted life year (DALY), health risk/impact assessment, occupational health, environmental health**

tativa di vita aggiustata per qualità persa per ogni caso. I risultati hanno mostrato che la contaminazione delle acque del terreno ha prodotto una perdita potenziale di 78 QALM (*quality-adjusted life months* = mesi di vita aggiustati per qualità) per le 1000 persone della comunità che vive a valle. L'entrata in vigore della legge sul casco a Taipei potrebbe salvare 6240 QALY per anno. L'inabilità attesa nei figli di lavoratrici del piombo era di circa 216 QALY. Se la qualità di vita fosse misurata in psicometria, essa potrebbe essere utilizzata nella valutazione dei risultati clinici. Se fosse utilizzato per considerare il costo delle malattie, potrebbe essere stimato il carico finanziario per la Previdenza Sociale. Concludiamo che il metodo è utilizzabile per una valutazione comparata rischio/impatto per decisioni di salute pubblica e politica sanitaria. Eur. J. Oncol., 13 (1), 33-39, 2008

Parole chiave: **qualità della vita (QOL), anno di vita aggiustato per qualità (QALY), anno di vita aggiustato per invalidità (DALY), determinazione del rischio/impatto sulla salute, medicina del lavoro, medicina ambientale**

Quantification of burdens of diseases

Beginning in the late 1960s, the integration of quality of life (QOL) and survival for quantification of healthy life expectancy was first proposed for the evaluation of healthcare of chronic renal disease[1]. It has been developed into a summary measure for population health[2] over the following several decades, with quality-adjusted life year (QALY) and/or disability-adjusted life year (DALY) as the common unit. Since the quantification of QOL for different countries may take too much time and resources and there might be different value systems because of different cultures in different nations, Murray *et al* proposed to consider simple adjustment for disability, or physical domain of QOL, of which the DALY evolves as the common unit for international comparative health risk assessment[3]. They have successfully quantified burdens of different diseases related to different health risks for international comparison.

However, since the DALY approach assumes a universal life expectancy and utility values for disability, which do not reflect the actual condition for each country or state, the direct application of such calculations for health policy decision at country and/or company level may not be feasible. Alternatively, we may re-consider the original question of risk assessment in environmental/occupational health, which we often come across, with a similar question of comparing overall health impacts of nephrotoxicity with hepatotoxicity or carcinogenicity in selecting a less toxic agent for substitution of an existing occupational or environmental hazard, namely, comparing different potential health impacts of diseases that might result from exposures to different chemical agents.

Risk/impact assessment: likelihood of the event multiplied with consequence of the event

Among different definitions of risk, the British Standards Institute BS8800 considers the risk as not only the quantification of likelihood of the event, but also the consequence of the event[4]. In fact, risk is defined as the multiplication of both factors. While experts of risk usually pay more attention to the likelihood or probability of the occurrence of event, lay people generally think of the consequence as the major concern. To quantify the consequences of different health events or diseases for comparison, however, one must quantify the changes or loss of life expectancy and QOL after the occurrence of different types of the health events or diseases. Namely, one should quantify both the life expectancies and QOLs with and without the occurrence of the event or disease and compare them, which had better be conducted under the same unit, and the QALY is one of the choices. While the life expectancy of the disease may be obtained through the long term follow-up of a cohort of patients, the QOL function usually must be surveyed in a sample of patients with the disease. Then, the life expectancy for the patients can be multiplied with the overall mean of QOL to obtain a crude estimate of QALE (quality-adjusted life expectancy).

However, because the QOL of patients actually fluctuates along with time after development of the disease, simply taking the overall average may not represent the dynamic changes of such time course. To more accurately estimate the QALE for the disease x_i, one can collect the QOL data from a cross sectional sample of patients to calculate the mean of QOL at each time point t_i through the smoothing method[5]. The mean QOL is thus multiplied with the survival probability for each time point t_i, and the lifetime summation of these values, or the total sum of area under the quality-adjusted survival curve, is the QALE of patients with disease x_i under the unit of QALY, if the measurements are taken yearly, as shown in fig. 1, or as follows:

$$\text{QALE} = \int E[Qol(\text{t}\,|x_i)]S(t\,|x_i)dt$$

Because the QALE of people without disease can be easily obtained through the life table of vital statistics of the general population and the QOL of the general population can be assumed as one, the consequence of the disease (or, loss of QALE) can then be obtained from computing the difference between the QALEs with and without the disease (condition expressed as x_0). Or, the consequence of utility loss because of the disease can be expressed as follows:

$$\int E[Qol(\text{t}\,|x_i)]S(t\,|x_i)dt - \int E[Qol(\text{t}\,|x_0)]S(t\,|x_0)dt$$

Because many patient cohorts with a specific disease may not have been followed for a sufficiently long time, especially chronic diseases, we might often end up with data with a high censored rate and may be unable to obtain the lifetime survival function.

Thus, we have developed a method for the extrapolation of the survival function of disease x_i, when the follow-up period may not be long enough or with a highly censored rate, i.e. over 50%[6], and demonstrated its validity in several real examples[7-10].

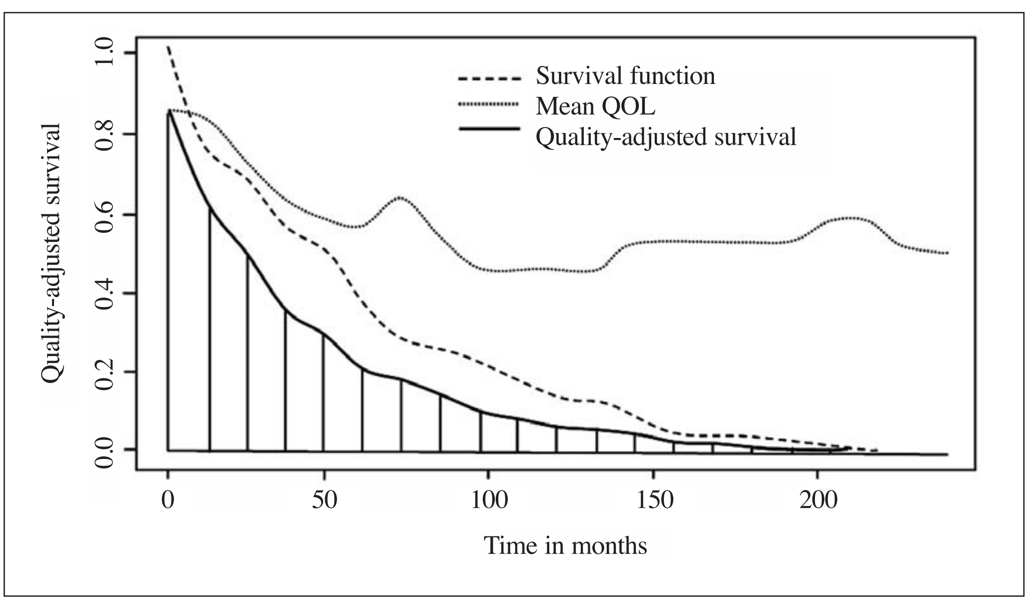

Fig. 1. The survival probability, mean quality of life (QOL), quality-adjusted survival of patients with disease, and the quality-adjusted life expectancy[a, b]

[a] Modified from Hwang *et al*[5]
[b] Quality-adjusted life expectancy = the total sum of shadowed area under the quality-adjusted survival curve

Let us take a real example of quantifying the loss due to the development of hepatocellular carcinoma (HCC), a prevalent cancer in Taiwan. We first established a cohort of about 2600 such patients in the National Taiwan University Hospital and followed them for 5 years to estimate the survival function of HCC. A cross sectional survey of 161 HCC patients with utility value of their QOL[11] provides expected value or mean at each time t_i, which can serve to adjust the survival curve. The area under the quality-adjusted survival curve is the QALE for HCC. Then, to each patient with HCC, we may apply a Monte Carlo method to simulate an age-, gender- matched person with the survival function (or hazard function) of the general population from the national vital statistics and produce an average survival curve of the reference population without HCC, of which the QOL value can be assigned to be 1. Then, the difference between these two QALEs is the area between the two quality-adjusted survival curves, or 233.6 quality-adjusted life months (QALM), which is the consequence of developing HCC, as shown in fig. 2. The equation can be regarded as a special condition of lifetime utility for the health condition x_i or, replacing the QOL function by a general utility function, as proposed by Freeman[12]:

$$\int E[U(t|x_i)]S(t|x_i)dt$$

Examples

To apply such an assessment in occupational and environmental health, one simply multiplies it with the likelihood or probability of developing HCC after exposure to a certain hazard or risk factor. For example, one of my studies tried to evaluate the potential health impact of pollution of underground water by dumping of chlorinated solvents on the ground, which occurred in an electronics manufacturing company X. After measuring the concentrations of 7 major pollutants including vinyl chloride, trichloroethylene, and tetrachloroethylene, from water samples of 43 local wells downstream of the dump, we were able to apply the calculation results of reasonable maximal exposure (RME) recommended by the US Environmental Protection Agency (EPA) and the cancer slopes obtained from related databases to obtain the expected likelihood of liver cancer, as briefly summarized in Table 1[13]. Namely, the estimated likelihood of developing liver cancer from underground water pollution of vinyl chloride, trichloroethylene, and tetrachloroethylene were 8.4×10^{-6}, 1.4×10^{-4}, and 1.9×10^{-4}, respectively, based on cancer slopes and the estimated RME obtained from measurements of water samples. As the population at risk in the exposed downstream community consisted of about 1000 people, we esti-

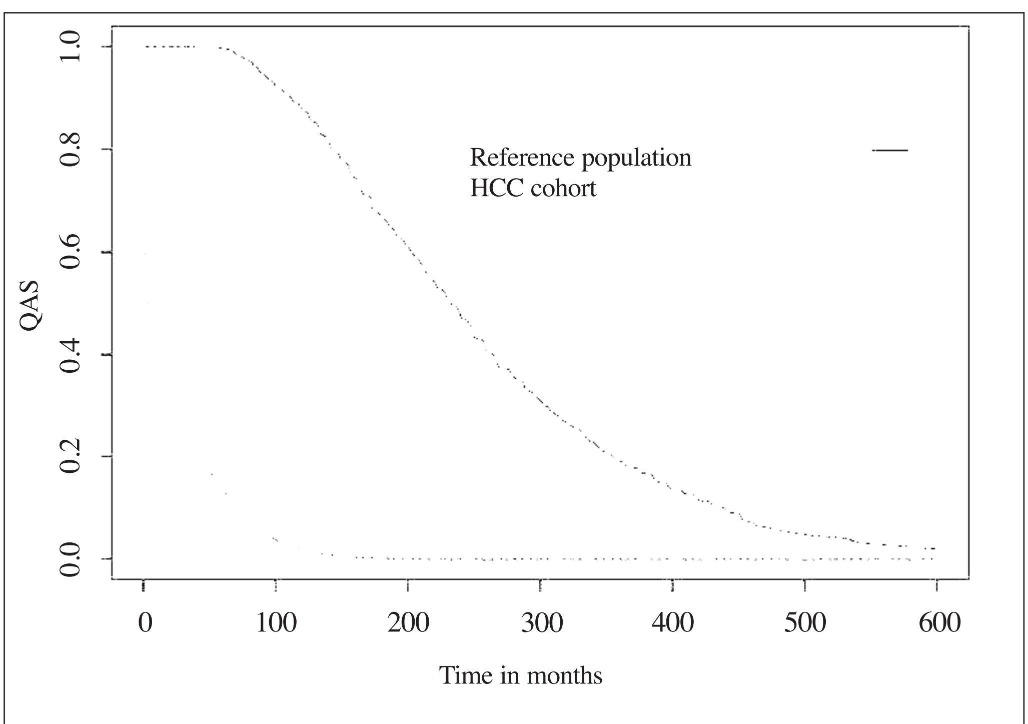

Fig. 2. The difference (shadowed area) of quality-adjusted life expectancy (QALE) between the cohort of liver cancer and age-, gender- matched reference population, which represents the average utility loss of developing a case of liver cancer, or 233.6 quality-adjusted life months (QALM)

Table 1 - Estimated health impacts of ground water pollution by selected solvents dumped on the ground by an electronics manufacturing company in Taoyuan, Taiwan[a]

Pollutant	Likelihood of liver cancer	Loss of QALM
Vinyl chloride	8.4×10^{-6}	2
Tetrachloroethylene	1.9×10^{-4}	44
Trichloroethylene	1.4×10^{-4}	32

[a] The expected likelihood of liver cancer is calculated based on a survey of water samples taken from all 43 wells downstream of the dump, cancer slopes from toxicology databases, and the reasonable maximal exposure recommended by the US Environmental Protection Agency[13]. Since the size of the exposed community was about 1000 people, the expected losses of quality-adjusted life months (QALM) due to different pollutants were also calculated based on the lifetime loss of health utility for a case of liver cancer, which is about 233 QALM, as shown in fig. 2.

mated that the potential health impact would be a loss of 2, 32, and 44 QALM (quality-adjusted life months), accordingly, assuming that there is no significant synergistic interaction among different pollutants, and that the total health impact would be 78 QALM.

A second example is the estimation of health impact resulting from enforcement of the helmet law for motorcycle riders in Taipei city. The proportion of motorcycle riders wearing a helmet was about 12% before 1996[14], while that after the law was enforced in 1997 improved to 95%. This increase in wearing of helmets was estimated to have reduced 1300 cases of head injuries in Taipei city annually. Based on the registry data of head injuries and followed for 7 years, the estimated lifetime consequence of such a case is a loss of 4.8 QALY, and the total impact of enforcement of the helmet law in Taipei city would save a loss of 6240 QALY per year[15].

The third example is the estimation of utility gained from different occupational health policies aimed at protecting the offspring of female lead workers[16]. The blood lead level measured in 1991 for female lead workers in Taiwan showed that about 331 out of 649 workers had a blood lead level exceeding 30 μg/dL. Assuming that the blood lead of each offspring is equivalent to that of his/her mother, there would be a mild utility loss among newborns because of mild impairment of intelligent quotient (IQ) resulting from increased lead absorption. According to the current literature, a blood lead level of over 30 μg/dL might produce a lifetime (namely, 74 years in Taiwan) IQ damage and a loss of utility of 0.116 for every offspring, while that of between 10-30 μg/dL might result in a reversible or temporary loss (assumed to recover after 2 years and a utility loss of 0.04 annually) based on the utility value taken from the Index of health-related quality of life[17]. Thus, the total expected utility loss for offspring of female lead workers would be 216 QALY. An improvement in occupational hygiene to reduce 10 μg/dL of blood lead would result in a saving of 89.2 QALY. Alternatively, if the lead factories established a policy of raising the employment age of female workers by 5-10 years, then the policy would have a similar impact, but would also violate the fundamental principle of equal employment opportunity. During the period between 1991 and 2001, the actual improvement of occupational health measures in the workplace regarding lead exposure reduced the blood lead level to an average of about 10 μg/dL[18].

Extension to the estimation of financial burden of an occupational and/or environmental health risk

The method can be extended into calculating the direct medical cost of illness paid by the National Health Insurance. Based on the data retrieved from the reimbursement data file, one can calculate the average financial burden for disease x_i for each time point t_i. It can be multiplied with the survival probability at each time point t_i and summed up to estimate the lifetime cost for different diseases after considering the annual discount rate. We have demonstrated the feasibility on the top 17 cancers in Taiwan[19], HIV/AIDS (human immunodeficiency virus/acquired immunodeficiency syndrome)[20], thalassemia[9], etc. For example, the monthly average medical cost paid by the National Health Insurance in Taiwan for maintenance haemodialysis was about US$1,576. By multiplying this average cost with the monthly survival probability, adjusting for annual discount rate of 2%, and summing up throughout life, we can obtain a lifetime medical cost for a typical case, which was about US$130,000. The total lifetime cost of a disease x_i can therefore be expressed as follows:

$$\int E[Cost(t|x_i)]S(t|x_i)dt$$

with the QOL function at time t replaced by the cost function, denoted as $Cost(t/x_i)$. Since the lifetime cost is simply the financial burden of the disease, we would multiply it with the likelihood of the event, or probability of occurrence of the event, to come up with the potential health impact in monetary terms for a particular occupational/environmental health issue. In fact, we have tried to demonstrate that the loss of utility due to smoking includes at least the financial burden of smoking-related diseases, impaired QOL, and premature mortality or shortening of life expectancy[21].

Extension to outcome research in clinical medicine and other possible environmental health settings

The method can also be extended to the measurement of QOL by psychometry, with the unit changed to score-time or score-year[22]. Unlike the measurement of QOL under the expected utility theory, there might be conditions under which a patient would rather die than live uncomfortably with the disease x_i. In other words, there might be health conditions that are worse than death in QOL. Thus, we must add another term for the score-time saved of the deceased, and the equation becomes as follows:

$$\int E[Qol(t|x_i))S(t|x_i) + (1 - S(t|x_i))\delta]dt$$

in which a constant δ is assigned to the QOL of the deceased for sensitivity analysis. This method was demonstrated in a study comparing the quality-adjusted survival of patients with and without bone marrow transplantation after chemotherapy for leukaemia[23]. But a score-time may not be directly linked to any particular meaning in life. Thus, we have tried to quantify the monetary value that a worker might be willing to pay for a unit of score-time in a study for the removal of physical pain resulting from permanently disabling occupational injuries with the contingent valuation method[24]. Namely, we have shown that workers in Taiwan would be willing to pay about US$65-70 for a painkilling pill with an effect lasting for 24 hours. The modification can also be applied to other environmental health settings that involve only loss of QOL for risk/impact assessment.

Conclusion

The integration of survival with the measurement of QOL can be summed up for the estimation of the consequences of different health events or diseases with the unit of QALY, which can be multiplied with the likelihood of the event in usual risk assessment to obtain the expected health impact. When the medical cost can be estimated for the specific disease for each time point t (say, monthly or yearly) based on the reimbursement database of the National Health Insurance, we are able to calculate the lifetime financial burden for a specific hazard after summing up the lifetime medical cost for the disease. The concept and method are useful for comparative risk/impact assessment in occupational and environmental health in order to take proactive prevention. Moreover, when the QOL measurement is replaced by psychometry, it can also be applied to clinical decision making and possibly other environmental health settings.

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