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The effect of antipsychotic drugs and non-drug therapy on borderline and psychotic mentally ill patient's quality-adjusted life-years (QALY)

Søren Ventegodt, MD, MMedSci, EU-MSc-CAM*[1,2,3,4,5], Niels Jørgen Andersen, MSc[4], Isack Kandel, MA, PhD[6,7] and Joav Merrick, MD, MMedSci, DMSc[5,7,8,9]

[1]Quality of Life Research Center, Copenhagen, Denmark;
[2]Research Clinic for Holistic Medicine;
[3]Nordic School of Holistic Medicine, Copenhagen, Denmark;
[4]Scandinavian Foundation for Holistic Medicine, Sandvika, Norway;
[5]Interuniversity College, Graz, Austria;
[6]Faculty of Social Sciences, Department of Behavioral Sciences, Ariel University Center of Samaria, Ariel, Israel;
[7]National Institute of Child Health and Human Development;
[8]Office of the Medical Director, Division for Mental Retardation, Ministry of Social Affairs, Jerusalem, Israel
[9]Kentucky Children's Hospital, University of Kentucky, Lexington, United States

Abstract

It is impossible for patients, physicians and health-politicians to know, which treatment to choose if the treatment outcome is not in one integrative measure. To evaluate the total outcome of the treatment of borderline and psychotic mentally ill patients with antipsychotic drugs compared to non-drug treatments, we choose the two major outcomes "quality of life" (QOL) and "survival time" integrated into one total outcome measure, the Quality-Adjusted Life Years (QALY).

Methods: We estimated total outcome in QALY (Δ QALY) by multiplying the estimated difference in global QOL (Δ QOL) and the estimated difference in survival time (Δ survival time): $\Delta\ QALY = \sum_{all\ outcomes}(\Delta QOL \times \Delta\ survival\ time)$. We included factors like suicide and spontaneous drug-induced death that is normally not included in clinical randomized trials of antipsychotic drugs.

Results: We found that the total outcome of treatments with antipsychotic drugs was about –2 QALY; the total outcome from non-drug therapies (psychodynamic psychotherapy, clinical holistic medicine) was about +8 QALY.

Conclusions: When the total outcomes of the treatments were measured in QALY, antipsychotic drugs harmed the patients, while the patients benefited from the non-drug therapies. Antipsychotic drugs violate the medical ethics of Hippocrates, "First do no harm"; non-drug therapy is therefore the rational treatment for the borderline and psychotic mental illnesses. Treatment with antipsychotic drugs is only justified, when prolonged non-drug therapy has failed.

Keywords: Psychiatry, mental health, quality of life, holistic health, antipsychotic drugs, clinical holistic medicine, suicide, adverse and side effects, spontaneous drug-induced dead, QALY.

* **Correspondence:** Søren Ventegodt, MD, MMedSci, MSc, Director, Quality of Life Research Center, Classensgade 11C, 1 sal, DK-2100 Copenhagen O, Denmark. Tel: +45-33-141113; E-mail: ventegodt@livskvalitet.org

Introduction

To evaluate the total outcome in medicine there are two general outcomes of primary interest: *survival* and *global quality of life*. These two measures can easily be integrated into Quality-Adjusted Life Years (QALY) (1). A positive QALY-contribution comes from positive effects of a treatment, and a negative QALY-contribution comes from a negative effect, called the adverse or side effects, like for example the patient's death caused either by drug-induced suicide or by the toxic adverse effects. Recent studies on all mentally ill patients in Denmark revealed a high risk of suicide (2) and unexplained death associated with psychiatric treatment and antipsychotic drugs (3). NNT (number needed to treat) and NNH (number needed to harm) numbers have been calculated for the treatment with antipsychotic drugs (4) and for the non-drug treatment (5), and the NNHs have been added up to a total NNH (4,5). Only some aspects of effects and side effects were related to QOL judged from the empery from the QOL-research (6-10); the NNT and NNH related to global QOL were thus evaluated on an empirical basis to estimate the size of the impact on QOL both of the positive and negative effects, to find the total impact on QOL of the treatment. Then the treatments impact on survival was evaluated. All in all the results made it possible to estimate the total positive and negative impact of the two alternative treatments in the dimensions *QOL* and *survival time*. From this we calculated the QALY impact of the different treatments of mentally ill with antipsychotic drugs and without these drugs, to compare them and find the rational, evidence-based treatment.

The borderline and psychotic, mentally ill patients and their physicians can today choose between either a drug treatment or a non-drug therapy like psychodynamic psychotherapy (11-15) or scientific CAM (complementary and alternative medicine i.e. clinical holistic medicine) (16-18). Till this day many different outcomes and adverse effects have made the picture highly unclear to the patients, the doctor, and the political decision maker. This study aims to provide the integrated outcome data needed to make a scientific comparison of the therapeutic value of the competing treatments and thus the data needed for a rational choice.

Methods

The QALY analyses of the effect of the non-drug treatments were rather trivial; although we had no data on survival, we had no reason to believe that any patient's life was shortened because of non-drug therapy (5). Quite on the contrary it seemed the therapy would prevent suicide and prolong life, but no accurate data could be found, so we did not include this in our calculations. We found QOL to be improved (11), or more often positive effects indicating that QOL was improved for the mentally ill patients (6-8) including patients with schizophrenia (9,10), thus giving a positive QALY outcome of non-drug therapy for mental illness.

The analysis of the QALY outcome for the treatment of mentally ill patients with antipsychotic drugs was much more complicated, so we had to build it partly on a meta-analysis on the total outcome of antipsychotic drugs (4), and partly on other studies as there were factors difficult to include in the traditional effect study due to lack of data. Factors like suicide rates and spontaneous drug-induced over-mortality were most often not included in the randomized clinical trials, so this information needed to be collected from separate studies. So we build the QALY-meta-analysis on the outcomes of antipsychotic drugs, and included the factors that were not included in the studies, to get a more complete picture of the positive and negative effects of antipsychotic drugs. Thus the present analysis contains more information and therefore is likely to give a more accurate picture than the documentation provided by the pharmaceutical industry.

We estimated the total outcome in QALY by multiplying the estimated difference in global QOL and the estimated difference in survival time: Δ QALY= $\sum_{\text{all outcomes}}(\Delta\text{QOL} \times \Delta \text{ survival time})$. We made all estimations conservatively, to avoid adding a bias here. We estimated conservatively the average patient to be 25 years old at treatment start; we know that most persons with schizophrenia are diagnosed between 15 and 25 years of age. The antipsychotic treatment is normally continuing for the rest of the patient's life, which we conservatively set to last for 65 years (which is shorter than the average life span of about 75). We used the measure "global QOL" and not health-related QOL, which is not based on QOL-

theory, but only on ad hoc measures (19) and preferred values confirmed with many different measures to large values only confirmed by one measure. We avoided the problems related to QALY described in an earlier paper (1).

Results

Recent Cochrane meta-analysis has shown that all antipsychotic drugs share the effect profile of chlorpromazine with a similar toxicity (20). We only found the outcome "mental state" relevant to QOL, as "relapse", "behavior" and "global state/global impression" all related to behavior, or to a mix of behavior and mental state. For comparison a normal life in Denmark is 75 life-years (21) of a mean 70% QOL (12,13) equivalent to 52.5 QALY.

Antipsychotic drugs, positive QALY-contributions: For antipsychotic drugs we found no improvement in mental state in our meta-analysis of 79 Cochrane meta-analyses of antipsychotic drugs (4). The analysis included all relevant data on subjective dimensions like fear, agitation, hallucinations, confusion etc. None of the dimensions related to global QOL showed any improvement; thus the positive contribution from improvement of mental state was 0.00 QALY.

Antipsychotic drugs, Negative QALY-contributions: We found in our meta-analysis (4) that severe adverse effects were very common with antipsychotic drugs, on average every patient had at least 1.66 adverse effects (11). We know from an earlier study that people with one or two health problems on average have a global quality of life that is 74.2% compared to people without health problems who have a global QOL of 76.1% (12); the health problems is therefore associated with a loss of global QOL of 1.9% for as long as the drugs are taken, which is normally all life if treated with antipsychotic drugs. This sums up to a QALY impact of –1.9% QOL x 40 Years= -0.76 QALY.

2.04% of the patients in the schizophrenic spectrum committed suicide in direct connection to starting the drug treatment (during psychiatric admission) and another 2.80% committed suicide immediately after admission (0-6 month) (22) giving a total of 4.84% of the patients with psychotic mental illnesses committing suicide in connection to the treatment with antipsychotic drugs, which is standard treatment in Denmark. As these patients are normally young (estimated mean of 25 years) and life expectancy of at least 65 years (conservative estimate), with at least a QOL of 41.4% (schizophrenia) (the global QOL for schizophrenic patients in Denmark (13)), this sums up to a QALY impact of –4.84% x 41.4% QOL x 40 Years= -0.80 QALY.

We know that antipsychotic drugs is associated with an 25% increased likelihood of unexplained sudden death, which normally is about 0.3% a year (23) and this continues for every year the drugs are taken; this sums up to a total of 40 years x 0.25 over-mortality/year, equal to10 times the normal mortality from spontaneous death of 0.3%; each death takes in average 20 years from the persons life. The total likelihood for spontaneous death is thus 3%. This sums up to a QALY impact of -3% x 20 years x 41.4% QOL= -0.25 QALY. The total QALY outcome of antipsychotic drugs is –1.81 QALY (see table 1).

*Non-drug therapy, positive QALY-contributions:*Psychodynamic psychotherapy have in uncontrolled studies cured 1/3 to 1/8 of the schizophrenic patients (9,10) and clinical holistic medicine have cured 57% of patients who felt mentally ill (11); a conservative calculation of non-drug therapy gives us a permanent improvement of QOL of 20%; the QALY contribution is thus 40 years x 20% QOL = 8 QALY. The 20% improvement in global QOL is conformed by measuring the global QOL before, after and one year after non-drug treatment (11,24).

Non-drug therapy, negative QALY-contributions: Adverse effects are generally considered not to be a problem in non-drug therapy, and suicide is very rare and actually more likely to be prevented that to be provoked (5-11,25). There is no indication of spontaneous death happening more often that usual (5). Conservatively estimated the QALY contribution from this is +0.00 QALY. The total QALY outcome from the non-drugs treatment psychodynamic psychotherapy and clinical holistic medicine is thus about 8 QALY (see table 1).

Table 1. QALY outcome from treatments with antipsychotic drugs and the non-drug treatments (PP= psychodynamic psychotherapy; CHM= clinical holistic medicine)

Treatment	QALY contribution
Antipsychotic drugs, positive treatment effect	+ 0.00 QALY
Antipsychotic drugs, adverse effects	-0.76 QALY
Antipsychotic drugs, suicide	-0.80 QALY
Antipsychotic drugs, spontaneous death	-0.25 QALY
Total QALY contribution, antipsychotic drugs	-1.81 QALY
Non-drug treatment (PP, CHM), positive treatment effects	+8.00 QALY (ref)
Non-drug treatment (PP, CHM), adverse effects	- 0.00 QALY
Non-drug treatment (PP, CHM), suicide	+ 0.00 (preventive effects, size unknown)
Non-drug treatment (PP,CHM), spontaneous death	- 0.00 QALY
Total QALY contribution, non-drug treatment (PP, CHM)	+ 8.00 QALY

Discussion

The method of QALY has been criticized because of the many different ways QOL can be measured (1), giving very different results depending on the QOL-measure. We find this critique to be correct when it comes to health-related QOL; we have therefore measured global QOL in 11 different ways (12-15,19) and have learned that the measure of global QOL is fairly robust, and surprisingly independent of theory and composition of questions in the questionnaire (12,13,19).

This means that global QOL can bee seen as a real, measurable phenomenon, and the measure of global QOL as an expression of a person's global state of life. The multiplication of global QOL and life years have been criticized also for being to simple; a long life with poor quality of life could be worse than being dead (1) and suicide could therefore be a rational act. We do not find any of these considerations conflicting with our estimations. We conclude that the presented conservative estimates are fair and free from bias.

Conclusions

In the treatment of the psychotic mentally ill patient, the total outcome of the treatment with antipsychotic drugs is -2 QALY, while the total outcome of non-drug therapies (psychodynamic psychotherapy and clinical holistic medicine) is +8 QALY (see table 1). The treatment with antipsychotic drugs is harming the patient, while the treatment with the non-drug therapy is beneficial judged from a QALY analysis. We must therefore strongly recommend non-drug therapy to patients with borderline and psychotic mental illnesses, whenever possible and warn against the extensive use of antipsychotic drugs.

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