DGSP Memorandum on the Use of Neuroleptics
The German Society for Social Psychiatry (Deutsche Gesellschaft für Soziale Psychiatrie DGSP) is the largest independent interdisciplinary association for anyone who works or volunteers in the field of psychiatry. Since its foundation (1970) it advocates improvements in the treatment of mentally distressed people and supports their integration into society.

Do you want to advocate a social psychiatry as well?
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Become a member and make a difference in psychiatry!

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Dear reader,

For many years the DGSP (German Society for Social Psychiatry) has been intensely engaged in the issue of the use of neuroleptics when it comes to the treatment of mentally ill people. Our member’s magazine “Soziale Psychiatrie” looks at this issue from different perspectives by people working in psychiatry and by users/consumers/survivors.

The use of neuroleptics has been widely discussed at several regional and federal interdisciplinary DGSP meetings and events with the participation of users/consumers/survivors and their family members.

At an expert hearing in 2009, at which several organizations participated, our positions regarding this issue were evaluated and the memorandum was rounded off.

This memorandum is the result and the future development of this intensive debate in Germany. It wants to encourage further discourse in our country regarding psychopharmacological therapy, which is a very important question for mentally ill people.

The memorandum shows our critical position and offers much information for family members, users/consumers/survivors and professionals.

Our organization is member of Mental Health Europe. With this English version we therefore wish to offer broad information and extend an invitation to discussion across Europe – with EU-officials, committees, working groups, our own MHE-member organizations and especially with users/consumers/survivors groups and their family members. We invite you to write your replies and your suggestions.

The umbrella organization MHE - with psychiatric community care as a focal point - supports the memorandum and welcomes the European distribution of the memorandum.

We hope for a lively discussion!
Cologne, Mai 2013

German Society for Social Psychiatry (DGSP)
The Board of Directors

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1 Introduction

In the early fifties psychiatric pharmaceutical research discovered a chemical substance (chlorpromazine). This agent and its many modifications known as neuroleptics led to astonishing positive effects for mental disorders. From this evolved a treatment optimism that was reflected in the psychiatric reform of the seventies and eighties. However, it was overlooked that only some people suffering from mental disorders benefited from these neuroleptics. Its use was also associated with considerable side effects, particularly with the life long administration. Later on it was hoped to overcome the scepticism of patients by introducing depot preparations (intramuscular injections with long lasting effect). The euphoria was quickly followed by disillusionment.

Even a “new generation” of neuroleptics failed to live up to the high expectations of these medications. They were called “atypical” because of their alleged fewer side effects. But soon they showed new, different, but not any less serious side effects. Unfortunately, psychiatrists in the past continued to be impressed by the pharmaceutical industry’s claims of “new and improved” drugs. Their naïve belief in progress - tied to the involvement of a partially corrupt scientific establishment - contributed to the neglect of developing alternative therapies. Recovery research results show a broad spectrum of individual therapeutic possibilities to manage without neuroleptics in the long term.
Neuroleptics are among the most profitable medications nowadays. For example in Germany in 2010 Quetiapine (Seroquel) was in fifth place of individual compounds, that is a 25 percent sales increase compared to the previous year (according to Barmer GEK- drug report of June 2011, page 33).

This level was achieved particularly because of the ever expanding area of application.

The DGSP is watching this trend with great concern. The results of the interdisciplinary meeting in March 2009 were gathered and summarized in this memorandum. With this second edition we publicly present our position for debate again. With it we present the results of a topical literature evaluation based on trialogical background experience (participation on an equal footing). Therefore the memorandum reflects the discussion between scholarly and professional psychiatrists as well as other professionals working in psychiatry, but also with family members of mentally ill people and last but not least with users and survivors of psychiatry.

We do not wish to demonize neuroleptics as a rule. We know that they can be of significant help in case of serious emotional distress when used carefully. We advocate modest and careful treatments. We caution against their excessive use, the neglect of alternatives and the downplaying of their side effects. We encourage empowered choices while considering the pros and the cons. We especially demand a pharmaceutical research independent of economic interests.

We would like to see psychiatry respect the dignity of the suffering person and the “freedom to illness” on the basis of trust and respect that helps the person gain a self-determined way of life that is agreeable to him or her.

2 Difficult trends in today’s psychiatry

2.1. Psychiatry’s biological reductionism

The past decades in the field of psychiatry were marked by the dominance of a largely biologically based understanding of mental disorders and their treatment. This was promoted by new neurobiological findings and the hopes for solutions of biological causes of mental disorders.

This one-sided interpretation of neurobiological research results that mental disorders are purely biologically based, are no longer consistent with current neurobiological science. Complex neurological models today show especially the interdependence between biological systems, social and ecological environment and the subjectivity of emotional experiences. Emotional and social experiences are structurally reflected in the brain as well. Scientifically
it is beyond dispute that psychotherapy and traumatic experiences lead to structural changes in the brain. The dominance of biological treatments is no longer justified. The genetic determinism was refuted by findings, which say that mental disorders requiring treatment are caused by complex gene-environment interactions. However, concepts that do not adequately reflect neurological processes in their interactions with the environment continue to determine the treatment practice. Therefore psychiatry frequently resorts to pharmaceutical therapies. The result is a psychiatric education solely based on medication compliance and biological explanations.

2.2 The increase of neuroleptic* administrations

The prescriptions of neuroleptics have been on the rise in the last few years. New substances were viewed and marketed as considerably less harmful. The range of application of different neuroleptics was significantly expanded. In the US neuroleptics have become top-selling substances among all medications now. The approval of the use of atypical neuroleptics for affective disorders constitutes an extension of indication. It is inadequately evidenced-based in the long term. Side effects like neurodegeneration and the metabolic syndrome were not appropriately taken into account.

Increasing off label prescriptions present one of the biggest problems, i.e. the administration of these medications for disorders and age groups for which they are not approved. Neuroleptics for borderline disorders are a common example for this. This may result in serious damage especially in older and young patients because of their physical condition.

* Later on the term “antipsychotics” was introduced. However that term seems inappropriate to us. It suggests healing, while neuroleptics can merely suppress symptoms.

2.3 The influence of the pharmaceutical industry on psychiatric research and practice

The criticized trends are in connection with the increased pharmaceutical influence on research, on medical further training and on the prescribing behaviour. The huge conflicts of interests of leading sales representatives in the field compromise the independence of psychiatry as a science and in practice as well. The integrity of the medical profession is suffering. An independent evaluation of medication is no longer possible.¹ The renowned organization Transparency International speaks of a “structural corruption” in the health care system given these conflicts of interests.² In Anglo-Saxon countries the conflicts of interest of academic research institutes and key opinion leaders are widely discussed among experts in the field as a
serious problem. Meanwhile many renowned universities in the US are
developing constructive resolutions to limit the influence of the
pharmaceutical industry on medical science. The same discussion has also
started here, for example with the forming of the initiative MEZIS (“mein
Essen zahl ich selbst” – “I pay for my own lunch” – an initiative of
incorruptible doctors).

Meanwhile the pharmaceutical industry finances and controls over 80% of
clinical studies. Literature about one-sided interpretations, selective
disclosures, withholding of negative study results, manipulations of study
designs and results make it impossible to get a clear picture. Many doctors
do no longer know what is reliable. Renowned scientists make no secret of
their fundamental scepticism towards many of the industry’s sponsored
studies.3 Examples of these developments can be found in the appendix
(see page XX, paragraph A and B).

2.4 The administration of neuroleptics to young children and youth

In Germany as well as in other western countries prescriptions of
neuroleptics to children continue to rise.4 That development is clearly shown
in the following chart.5

| Outpatient prescription of some “atypical” neuroleptics to children (Germany, GKV, Health Insurance Association) in the years 2001 and 2006 in defined daily doses (DDD) per 1000 insured according to age groups |
|--------------------------------------------------|----------|-------|-------|
|                                                  | 5 to 10 years | 10 to 15 years | 15 to 20 years |
| 2001                                             | 2006       | 2001 | 2006 |
| Risperidone                                      | No data    | 29.8 | 2.5  | 89.4 | 50.7 | 138.6 |
| Olanzapine                                       | --         | 10.1 | no data | 18.1 | 59.1 | 69.0 |
| Quetiapine                                       | --         | no data | -- | no data | 25.0 | 66.7 |
| --                                               | = No prescription |
| No data = No information or rather number of prescriptions less than 1000 |

Children and youth on atypical neuroleptics show an alarmingly faster weight
gain as well as metabolic changes in comparison to adults.6 Studies
document distinct early and lasting metabolic side effects. This casts doubt
on the popular use of atypical antipsychotic medication for children.8 (A
more detailed DGSP comment on the use of psychotropics for children and
youth with particular reference to an ADHD diagnosis will be published shortly.)

2.5 The administration of neuroleptics to people who are mentally disabled

More than half of mentally disabled people living in care facilities are administered psychotropics often without clear indication. According to newer studies the administration of neuroleptics for the treatment of behavioural problems in people with mental handicaps or with autism should be assessed sceptically because of the lack of effectiveness and the negative side effects.9 Neuroleptics are used too easily when dealing with mental retardation and challenging behaviour. We welcome that the German Society for mental health of mentally disabled people (DGSGB) continues to critically address this development. Also the effectiveness of drug free interventions is stressed. The need for scientific research is emphasized. It is desirable that psychiatry devotes the same attention to this group of people. A less pharmacological, but rather a psycho-socially oriented understanding of difficult or challenging behaviour in mentally disabled people is urgently needed as well.

A project sponsored by “Aktion Mensch” imparts favourable examples, i.e. how mentally disabled people with the help of a multi-professional team can achieve a reduction of psychotropic drugs. By now several disabled people manage to a great extent without any psychotropic drugs. More information can be found at www.ichwillmich.de.

We hope that preferable differentiation processes for the medication treatment of mentally disabled people will get addressed at the UN Convention on the Rights of Persons with Disabilities.

2.6 The administration of neuroleptics in old age and to patients with dementia

The prescription prevalence of neuroleptics for dementia patients appears relatively stable after a slight decline from approximately 35 percent to 32 percent from 2004 to 2006. Thus one out of three dementia patients received at least one prescription of neuroleptics in the observation period.

According to that the FDA warnings regarding serious adverse drug reactions of atypical neuroleptics in 2005 and of typical neuroleptics in 2008 as well as national warnings did not produce a noticeable decrease in the prescribing behaviour.

Since the FDA first warned in 2005 against the use of atypical neuroleptics for dementia patients, paradoxically, their prescription is on the rise.10 The highest rate of neuroleptics prescription per capita is for elderly people at
40 percent, in care level 3 (the highest care level in Germany) the rate is over 50 percent. This does not only apply to Dipiperon, Eunerpan and Risperdal, but for all medications of this substance group. Neuroleptics are by far the most prescribed group of psycho-pharmaceuticals to nursing home residents with dementia, in fact independent of the psychopathology of the residents.

The administration of neuroleptics to older patients is mostly done for behavioural control. Multi-morbid patients are frequently affected by these prescriptions. It is well known that the use of conventional and atypical neuroleptics in older patients increases the mortality risk, the risk of heart failure and strokes as well as the risk of cognitive deficits. So far the only randomized placebo-controlled study with 165 patients, who had all been treated with neuroleptics before the start of the study, showed the death rate significantly doubled after 36 months. 59 percent of the patients died in comparison to 30 percent of the patients who were taken off neuroleptic medication after the randomization.

In addition to the abovementioned reasons of increased mortality the following risks are associated with older people and people with dementia receiving neuroleptic treatments: pneumonia, extrapyramidal symptoms (EPS), thrombosis, cardiac arrhythmia and impaired ability to swallow, as well as impaired cognition, meaning the dementia symptoms intensify. The risks are to some extent interrelated (e.g. impaired ability to swallow – pneumonia – death; EPS – fall – death; thrombosis – pulmonary embolism – death). In many cases the rationale is sedation.

When it comes to non-cognitive dementia symptoms (e.g. restlessness or shouting) the effectiveness of neuroleptics is limited, meaning symptoms stay unchanged in spite of the medication in some patients. Therefore the medication does more harm than good.

Non-cognitive and challenging aggressive behaviour in people with dementia often recedes by itself. This is given too little thought by caregivers and in the prescription practice and is often mistakenly attributed to the medication. The administration of neuroleptics to people with dementia is almost like a reflex.

Non-drug interventions are not utilized as the guidelines of the German Society for Psychiatry, Psychotherapy and Neuropsychiatry (DGPPN) define.

Pilot studies of such strategies show promising evidence of their effectiveness. The Institute for Quality and Efficiency in Healthcare (IQWiG) pointed to the blatant absence of valuable research on this subject.

The essential issue is that neuroleptics get administered to people with dementia in situations in which they should not be used. Once administered it rarely gets checked to see if the treatment is still needed or if the dose is
still appropriate. Frequently an accumulation of adverse drug reactions develops that leads to higher mortality and morbidity in old age.

Serious risks that are downplayed by advertising encourages careless administration practices. Most neuroleptics are used off-label, i.e. prescribing doctors have an increased liability risk because neuroleptics are not approved for the treatment of dementia. A consultation with our pharmacist at the BfArM, however, revealed that he sees this differently.

In 2009 Eli Lilly was fined $1.415 billion dollars by the department of justice for off-label marketing. They had marketed the neuroleptic Olanzapine (Zyprexa) for dementia without approval (off-label). 20

Because of the pharmaceutical friendly legal position such lawsuit would not be possible in Germany.

3 The administration of neuroleptics for the treatment of people suffering from psychoses

Complex psychotherapy interventions are underrated or are not even offered when it comes to treating psychosis. The exaggerated expectations of the so-called atypical neuroleptics have given way to disillusionment, yet they continue to be administered as the main treatment element. Reasons for focusing on drug treatments is the overestimate of the drug benefits and the underestimate of the risks as well as the insufficient implementation of psychotherapeutic and alternative treatments.

Overrating the benefits

Since the introduction of neuroleptics the progress of schizophrenic patients in treatment has not fundamentally changed as long-term studies show. The percentages between “good”, “modest” and “poor” treatment results have only slightly changed in spite of better overall treatment conditions. Treatment successes with the help of psycho-social interventions were already in existence before the introduction of neuroleptics.21 The claim that the de-hospitalization was made possible by neuroleptics is unfounded. Newer efficacy studies also show poorer effects than the frequently quoted older studies as well as a decrease in effectiveness as the time goes on.22 (further important study results can be found in the appendix, paragraph C, page XX)
Underestimating the risk

It has been known for decades that movement disorders, mostly irreversible, are partially dose-dependant especially among typical neuroleptics. Only in the last few years has research been done on the increase of overweight, diabetes mellitus, fasting value of blood sugar, lipid metabolic disorder and cardio-toxicity. Increases of these side effects raise the somatic morbidity and thereby probably the long-term mortality in patients, too. The risk of sudden cardiac death is approximately the same with typical and atypical neuroleptics, though it is different for individual substances. See appendix (page XX) for further important aspects of side effects like metabolic syndrome, neurodegeneration and results of dopamine-receptor blockade.

Prevention and limits of early intervention with neuroleptics

The possibly sensible early recognition of psychotic disorders entails the danger of increasing ill-founded neuroleptic administrations. The transition of 10 percent to 40 percent of people with minor psychotic symptoms (so-called attenuated psychotic symptoms syndrome) to an acute psychotic disorder within one to two years does not generally justify neuroleptic medication. These actions lead to unnecessary false-positive ratings and hence to serious medical malpractices.

Furthermore there are diverse ethical problems when frequently the unjustified fear arises to develop schizophrenia. In such cases psychosocial treatment models are of significant importance. It is amazing that so far there are hardly any early stage diagnosis projects, which utilize proven therapies and the effects of family therapy regarding the relapse rate as well as the prevention of the first episode. It is even more surprising since most of the clients are in the late stage of adolescence and in individuation and separation processes from their families.

So far early intervention models focusing on drug treatment after the start of psychotic disorders have produced only inconsistent and limited, yet not lasting treatment outcomes. Furthermore additional risks of psychotic reoccurrences after preventative administration and especially after abrupt coming off neuroleptics have not been researched at all. Surprisingly, omega-3 fatty acids (fish oil) are more effective than neuroleptics according to current studies. Not the early pharmaceutical intervention, but above all psychotherapeutic and psychosocial treatment care appear to be of vital importance for early therapeutic intervention.
4 Further aspects of the treatment and care of patients with serious mental disorders in Germany

People with schizophrenic disorders continue to die 20 – 25 years earlier than the average population. The causes are diverse and not yet completely clear. In addition to unhealthy live styles and higher suicide rates, there is clear indication that drug treatments (depending on the substance and dosage, as well as taking several drugs simultaneously) contribute to the higher early death rate among people with mental disorders. (see appendix, paragraph D, page XX)

In spite of better treatment conditions and considerably higher drug treatment prevalence schizophrenia is in industrial countries in comparison to many developing countries a high-risk illness in terms of frequency of occurrence and progress. This provides food for thought regarding our treatment practice (see appendix, paragraph G, page XX f.). Screening of risk factors is called for (see appendix 6, #3, page XX).

Besides the prevention of suicide physical health including smoking and nutrition ought to have the same importance in everyday therapy. Even here there is great need for research in this area.

5 Counter-Movements: introducing primarily psychotherapeutic methods for the treatment of schizophrenia

In other European countries the latest research in neurobiology (see paragraph 2.1, page XX) and the stressing of psychotherapeutic interventions are reflected in mental health treatments. In Finland people have a right to psychotherapy even and especially psychotic patients. In Great Britain the British National Institute for Clinical Excellence (NICE) approved groundbreaking treatment guidelines for schizophrenia, which for example include mandatory behaviour- and family-therapy intervention for all patients. It is advised to stay away from an accepted basic psychotropic compliance therapy and a psycho-education without the inclusion of family members is not recommended.

In Germany, however, these insights find little support in practice. Psychotherapeutic treatments (e.g. family-therapy and cognitive behaviour-therapy) have been recognized for years as effective by scientific literature reviews (meta-analyses), yet are not implemented due to a lack of incentives. Most resources in psychiatry are tied to treatments of minor emotional disorders.
6 Necessary conclusions for the treatment of mentally ill people: demands by the DGSP

Psychiatry as a science and practice has to free itself from its exclusive biological focus and as an interdisciplinary social science has to understand, that biological, psychological and social approaches and their research methods are to be integrated equally. This way a properly understood and not a one-sided biologically based psychiatry is not a contradiction, but an important bridge to the different disciplines underlying psychiatry.

The foundation of a solid therapy for mental disorders is a complex psychosocial treatment. This treatment approach may administer neuroleptics in low dosages or avoid them entirely. Changes are needed in the following 10 areas:

(1) Psychotherapy and psychosocial help within psychiatric community settings

According to the above-mentioned arguments help for mentally ill people can only be adequately achieved by regional psychiatric community settings (community psychiatric networks). Outpatient, inpatient and day care forms of acute treatment, rehabilitation and integration must be able to respond to the different personal needs. This means in particular:

- The acute care of mental disorders should preferably take place in the person’s living environment, usually at home. The treatment focus must be on psychotherapeutic and psychosocial intervention and guidance. This applies to long-term treatments, rehabilitation and support as well. It is important to ensure a reliable and long-term relationship as much as possible.

- Interdisciplinary community based psychiatric care is to be rendered. Not only are medical competencies needed, but also psychotherapy, socio-therapy, nursing care, ergo therapy, art therapy, music therapy, exercise therapy, as well as social work competencies – to mention only the most important. Psychotherapeutic and community based psychiatric care is an essential requirement for all occupational groups in order to be able to work in this field within the network system.

- It is important to actively include psychiatric consumers/survivors as well as relatives as “experts”. Therefore mental health seminars and paid services from experts with lived experience as well as different kinds of self-help should all be part of the support system.
- Possibilities and access to interdisciplinary psychotherapeutic and community-based outpatient treatment options are to be developed and expanded in particular for acutely and chronically ill people.

- The securing of earliest possible integration in education and occupation and in meaningful activities by professional support in accordance with “supported employment” and “supported education” is of particular importance.

- Inpatient care ought to have an environment free of irritants, must be trauma sensitive and have crisis support.

- Public funds need to be available for patients to have access to innovative projects. These projects include the participation of survivors and family members, e.g. Soteria-facilities, need-adapted treatments and community-based outpatient treatment teams as alternatives to pharmacologically focused treatments.

(2) Neuroleptic Treatment: Indication - Dosage - Combination

- Requirement:
- Comprehensive treatment education including adverse drug effects and possible interactions as well as alternative treatment possibilities;
- Informed decision;
- Preferably selective and lowest possible administration of neuroleptics in appropriate therapeutic settings.32 Regarding this there are experimental studies of the “being-with” Soteria care-treatment and the Finnish need-adapted treatment model.33 With the help of such treatment models over 40 percent of first-episode patients with schizophrenia can achieve equally good if not better long term results without the use of neuroleptics. Approximately an additional 20 percent need them only occasionally. For others much lower than usual dosages are sufficient. Other mental disorders can be treated even more often without neuroleptics.
- Lowest possible acute treatment dose for patients with repeated episodes, who often manage on 3.3 – 4.0 mg Haloperidol equivalents daily.34 The required dose for first episode patients is lower: 0.5 – 2.0 mg Haloperidol equivalents daily.35 Exceptions are for example: CYP-450-extensive metabolizers (accelerated reduction of neuroleptics); pre-treated patients with excessive pre-medication who can only be slowly reduced.
- Patients are as much as possible to be included in the decision-making after detailed education about all relevant side effects and alternative treatment possibilities. Should a medical treatment be declined, this
must not automatically lead to question the patient’s capacity to consent.
- Increasing the dose slowly over weeks to find a minimal dose. Intermittent use of Benzodiazepine is often sensible and is less harmful than high dosages of neuroleptics.
- High doses only after strict and carefully justified indication.  
- Offering slow reduction and possible attempts to discontinue within the framework of psychiatric care and preferably psychotherapeutic treatment as well. For patients with infrequent episodes (less frequently than every 2 years) drug-free intervals can be more advantageous in the long run than the continuous use of medication. Psychotic episodes after complete remission can often be treated with low dosages or by taking Benzodiazepine over a few weeks.
- Avoiding the combination of several neuroleptics (poly-pharmacy). There is no scientific evidence for their better efficacy except for combination treatments with Clozapine in case of therapy resistance. It is also associated with an increased risk of adverse effects. Should poly-pharmacy appear to be appropriate in a given case, it ought only be taking place under strict supervision of cardiac and metabolic side effects as well as the QT-interval in the electrocardiogram (ECG). Of course patients are to be informed about the increased risk of adverse effects of a combination treatment.
- Working with treatment arrangements.
- Taking into account advance directives.

(3) Neuroleptic Therapy: Monitoring

- Regular checkups in accordance with the DGPPN (German Association for Psychiatry and Psychotherapy) S3-guidelines and the recently published guidelines for monitoring the drug treatment of patients with bipolar disorders. This applies to changing medications as well. Monitoring weight gain, overweight, blood pressure, checking for diabetes, elevated blood fat levels, prolongation of the QT-interval in an ECG, elevated prolactin and sexual side effects, motor disturbances, i.e. extra-pyramidal disorders and akathisia, tardive dyskinesia, cataract, myocarditis.
- Requests to reduce: In recent years psychiatry contributed considerably to the increased administration of neuroleptics therefore it is psychiatry’s obligation to provide expert guidance and support should patients request to reduce. In the long term patients should be continually motivated and supported.
- Non-responder: Patients in whom neuroleptics do not have the desired effect must be granted - at the latest after a treatment attempt with clozapine and possibly a second neuroleptic - the opportunity to reduce and eventually to completely discontinue under psychosocial guidance and support.
(4) Requirements for the competence of therapists and hospitals

- More psychiatric and pharmacological competence in regard to the treatment of multi-morbid, especially elderly patients with mental disorders.
- Non-medical professionals as well as legal representatives need to have a basic psychopharmacological knowledge.
- Use of intelligent software systems (Computerized Physician Order Entry, CPOE) for early detection of medication interactions and other risks associated with the administration of neuroleptics.
- The quality of pharmacological treatment and its continuous monitoring should be a criterion for the quality-standard of a hospital.
- Optimizing therapy by involving hospital pharmacists.
- Hospital discharge summaries must include reasons for a medication change, steps for future medication reduction on an outpatient basis, changes and adjustments.

(5) Improvement of general conditions

- Psychotherapeutic treatment options, low dosage treatment according to the current NICE guideline and treatment without neuroleptics must to be taken into consideration when it comes to the care.
- The right to a drug-free treatment approach even in the hospital. This requires a change of the health insurances’ medical service policies so that hospital care is not only based on the administration of medication, change of medication or complex medical treatment regimes.
- Revision of the DGPPN S3-guidelines ‘Schizophrenie’ in cooperation with other organizations and taking into consideration alternative treatment strategies.
- Addressing the aspect of ‘more safety when it comes to neuroleptic therapy’ in the action plan presented by the Federal Government designed to improve the safety of medical treatments (Arzneimitteltherapiesicherheit AMTS) in Germany.
- Comprehensive transparency rules when disclosing conflicts of interests between medicine and the pharmaceutical industry.
(6) Further training – Qualification – Information

- Compulsory continued medical education, which is independent of the pharmaceutical industry’s interest, for therapists in the use of neuroleptics and their dosage reduction as a firm component of the curriculum.
- No commercially sponsored training of scientific research in psychiatric institutions. Provision of funds, which are independent of the pharmaceutical industry, for further education and training.
- Qualifying measures in line with psychotherapy/social-psychiatry for all psychiatric occupational groups.
- Independent information systems about psychotropic drugs for doctors, patients and citizens in general.
- Regulations in dealing with pharmaceutical representatives in hospitals along the lines of the regulations of the Clinic for Psychiatry and Psychotherapy at the University Hospital in Mainz.

(7) Involving patients and relatives

- Mandatory participation and control by survivors/users and their relatives in organizing the care. This participation is needed and possible on all relevant levels of psychiatric care (advisors, complaints office, community based mental health association, psycho-social working groups, approval of user-led facilities, hiring of psychiatric survivors as employees etc.).
- There are now qualification programs of and for (ex-) users and survivors to act as experts from their own experience in the treatment of others (peer experts). Since 2005 the EU-funded project “Experienced Involvement” (www.ex-in.de) has laid the foundations for the employment of (ex-) users and survivors in the occupational field related to social psychiatry in Germany.

(8) Compliance with the UN-Convention on the Rights of Persons with Disabilities

Attention must be paid to the UN-Convention of the Rights of Persons with Disabilities. Establishing therapeutic services and therefore choices for users/survivors - in particular for the purpose of alternatives to psychopharmacological treatments or minimising them - is necessary in view of the UN-convention signed by the Federal Government March 2007. The common clinical practice of not granting people with serious or chronic
recurring mental disorders any decision making powers with regard to their therapy – with the argument that they lack insight – is no longer acceptable.

(9) Care structures and their funding

- Regional community based psychiatric associations of all relevant service agencies and service providers in responsible coordination by local authorities and regional community based psychiatric quality management that include psychiatric survivors and relatives are to be established or expanded.
- Regional planning of resources on the basis of the above.
- New remuneration systems that allow for acute care at the place of living including the social needs of patients and provide for qualified long term care, reintegration and recovery. Included in this are regional budgets, better integrated care, removal of the huge financial differences between the compensation for outpatient care versus inpatient care plus fewer incentives for the chronification of patients are of key importance.
- The Personal Budget (Persönliches Budget) has created a legal basis for more participation of people with disabilities. Investigations have shown that decisions made by users/survivors about their own goals and arrangements and their use of the available money are feasible. We demand removing administrative barriers and implementing the Personal Budget into practise in compliance with the law.

(10) Research

- An independent psycho-pharmaceutical research involving all relevant people, i.e. users/survivors and relatives, must be established. Independent research can be achieved following the practice of the American Universities Stanford and Yale. Their strict code of conduct prevents almost all direct financial contributions between the industry and the medical profession and academic centres with the exception of pooling financial contributions from the pharmaceutical industry, which then make uninfluenced training and research possible. In addition more publicly funded research is needed so that promising research approaches that do not profit the pharmaceutical industry are not left behind.
- Compulsory independent of industry implementation of Phase IV studies (randomized studies done under routine conditions) immediately following the approval of new drugs as a basis for drug reimbursement. For this purpose this should capture patient relevant parameters besides improving psychopathological symptoms, i.e. long-term quality of life and especially social inclusion.
- Mandatory reports of all clinical studies in a publicly available study register and prompt publication of the results after the study is completed.
- Research has to put more emphasis on non-drug therapies. Publicly funded studies and models of optimal psychosocial treatments of
serious mental illness that include the possibility of trying only minimal or no neuroleptics. This would correspond with recovery approach work and the UN-Disability Rights Convention. Such services must therefore be implemented in regular care.

Appendix

A. One-sided information, non-disclosure of study results, selective publication of studies due to extensive research control

90 percent of the drug trials are industry-dependent. 80 percent of industry-sponsored studies were still conducted by relatively independent researchers at universities in 1991. Now the pharmaceutical industry conducts 80 percent of the studies themselves or commissions private businesses with it (i.e. Clinical Research Organization, CRO). This allows the industry extensive control of its sponsored studies from design to publication.

This had serious consequences for the assessment and the administration of neuroleptics because the medical product of the sponsor was identified as the superior product in 90 percent of the studies on “atypical” neuroleptics. This was essentially achieved by the fact that 94 percent of American and 80 percent of British drug trials of the new “atypical” neuroleptics the control groups used conventional “typical” neuroleptics reference dosages, which exceeded the upper limit of the recommended dosages for these patients and often even exceeded the limits for seriously ill people. That lead to distorted side effects profiles in the control groups – to the detriment of older and cheaper substances.

It was only after years of delay that the results of the industry-independent CATIE study (2005) as well as the results of two other independent studies brought about the sobering re-evaluation of atypical neuroleptics. Even antidepressants had to be re-evaluated in 2008 because meta-analyses clearly indicated, when consulting previously unpublished data of evaluation studies, that the effectiveness of antidepressants is overrated, however side effects are underrated. The placebo effect turned out to be much higher than previously assumed. The reason was simple: of 36 studies assessed by the FDA (American Food and Drug Administration) with either negative or questionable results were all - except three - either not published or published in such a manner that they conveyed a positive result. In comparison only one of the studies with positive results was not published. By means of these selective disclosures the alleged effect size of the evaluated antidepressants increased by 32 percent overall. In case of mild and possibly moderate depression there is therefore no solid indication for a primary medical treatment any longer.

Selective publication and interpretation of research results have become a major misleading and distorted scientific problem that can lead the purpose of evidence-based medicine ad absurdum. Overall 50 percent of the effectiveness data and 65 percent of the data on harmful effects in
randomized controlled trials are published incomplete. Companies even refuse study results to national institutes like the Institute for Quality and Efficiency in Health Care in order to assess medications and treatments as part of their legal obligation.

Publishers of twelve leading medical journals declared 2001 that clinical studies are mainly conducted for marketing purposes. Often sponsors control design and data publication and the overt misuse of the studies was deplored. This makes the whole thing a farce and even reputable scientific journals are prone to misstatements.

B. Marketing
In Germany each year 2 billion Euros are spent on pharmaceutical representatives mostly for marketing purposes and one-sided information at the expense of health insurance funds and their contributors. More than 90 percent of the promotional material left by pharmaceutical representatives in doctor’s offices is either irrelevant, wrong, not proven or does not correspond with the literature details to which it refers. Approximately a third of the drug industry’s revenue is used for the marketing of medications. That is 2 to 3 times as much of what is used for research and development.

Marketing also includes the distribution of smaller and larger gifts to prescribers, the financing of conference participation for patients’ organisations and medical associations and the financing of the so-called observational studies, which usually have no scientific value. Many doctors are of the opinion that their prescription practice is not affected by this, however, studies clearly indicate otherwise. Equally disturbing is the fact that the pharmaceutical industry in several cases concealed considerable side effects of psychotropic drugs or announced them with significant delay.

For example the pharmaceutical company Lilly falsified data of the neuroleptic Olanzapine for the approval by the US Food and Drug Administration: the on-set of hyperglycaemia (increase of blood glucose level) from 3.6 versus 1.05 to 3.1 versus 2.5 “New York Times” December 17, 20 and 21 2006. A leak in the company presented the data to the public. As a result Lilly paid 1.2 billion US dollars to 26 000 diabetes victims as part of a legal settlement.

The pharmaceutical giant GlaxoSmithKline (GSK) withheld for five years the study results about the ineffectiveness of the antidepressant Paroxetine and its significant suicide risk when administered to children. This led the UK government at the EU level to call for more stringent laws against the suppression of study results.

Illegal requests by manufacturers aimed at off-label prescriptions have resulted in fines and compensation claims running in the billions in the USA. Various falsifications and deceptions have been made due to marketing interests. This created a situation in which reliable decisions regarding the administration of psychotropic drugs cannot be made.

C. Overestimating the benefits of neuroleptics
The meta-analysis by Hegarty et al. ‘One hundred years of schizophrenia’ revealed in 1994 that studies done prior to 1925, well before the discovery of neuroleptics including patients with less than 6 months of symptoms, 45 percent of the patients substantially improved over time while this applied only to 41 percent of the patients in the period from 1975 to 1994. If patients with less than 6 months of symptoms are excluded the percentage of improved patients increased considerably from 20 to 30 percent since the use of neuroleptics due to improved treatment structures, however, psychosocial therapies are also included in this increase.

Long term studies (between 22 to 32 years) that predate the advent of neuroleptics show comparatively high rates of recovery (between 46 to 68 percent, usually about 55 percent). A systematic review of 37 follow-up studies involving patients after their first schizophrenic or schizoaffective episode (all studies after 1980 and lasting on average 3 years) arrives at the following summary of results: of the 4100 patients 42 percent had good, 35 percent moderate and 27 percent poor treatment results. Additional psychosocial therapy was a predictor for positive outcomes. Studies of selective neuroleptic treatments were not included in the review.

The dehospitalization, which had already started in the UK before 1954, shows no significant increase after the introduction of neuroleptics. In the study on rehabilitation by Vermont only 25 percent of the dehospitalized and successfully rehabilitated patients continued taking neuroleptics on an on-going basis, 25 percent occasionally and 50 percent never.

Two current study overviews (see references, note 22), which mostly evaluate newer studies, clearly show limited efficacy of neuroleptics as well. Only a small improvement of positive symptoms is documented in these studies. The difference to the placebo control groups is also moderate. The number needed to treat (NNT) to reach the desired therapeutic goal is 6. Based on older studies the NNT used to be 3 to 4. Beyond that the efficacy of neuroleptics decreases in the process.

D. Underestimating the risk: metabolic syndrome

Weight and metabolic indicators at the onset of the disorder and before treatment correspond to values of a healthy control group. In the first year of neuroleptic treatments weight gains between 5 to 17 kg, depending on the type of the atypical neuroleptic, were reported in the analyzed studies. In addition there were diverse changes of insulin values and lipometabolism. The renowned journal “Lancet” commented on this overview as follows: “The combination of antipsychotic side effects with poor diet, physical inactivity, high rates of smoking and other factors associated with mental disorders, together with socioeconomic deprivation has a devastating effect on cardiometabolic health. It is no surprise that the lives of people with severe mental illness are 16 to 25 years shorter than that of the general population and that coronary heart disease, not suicide, is the major cause of death.”

Previously in the same journal a Finnish clinical trial registry appeared, in which patients on Clozapine and Olanzapine exhibited the smallest mortality rate and patients without neuroleptics the highest. However, in response
to this study a serious critique was published which the expert community hardly noticed.
A new British register study found that the gap in mortality rates between the general population and people with psychosis continued to increase between 1999 and 2006, especially after the age of 65 years. In particular cardiovascular diseases were cause for the increase. Smoking, obesity, neuroleptic medication, physical inactivity, diet and alcohol are discussed as causal factors in the literature.

E. Neurodegeneration
Several follow-up studies since 1998 show a reduction of the grey matter in the frontal lobe correlated to the cumulative dose of antipsychotics. There are eleven follow-up studies concerning this matter. Nine of these studies show evidence in different group comparisons of further reduction of the grey matter in people diagnosed with schizophrenia and taking neuroleptics. Two studies note an advantage of atypicals, three studies note no difference between typicals and atypicals, one study notes no more difference after one year.

Five studies investigate and prove a correlation between the reduction of frontal grey matter and cognitive disorders (attention, executive functions, verbal learning, working memory, problem solving skills, abstraction ability, spatial memory and visual spatial skills). The more the volume of the grey matter decreases, the more pronounced these cognitive disorders are. After the initial decline and relative stability between the second and the fifth year of neuroleptic treatment, there seems to be a further significant deterioration of neurocognitive capacities between the fifth and the ninth year.

Furthermore some studies identify as well a correlation between increased negative and positive symptoms and frontal lobe atrophy.

The latest and largest study investigated 211 first-episode schizophrenia patients over a period of 7 (up to a maximum of 14) years without a randomized control group. On average 3 MRI (magnetic resonance imaging) were performed on each patient.

“Not an ideal study design, however, this is the best we could ever arrive at something like that”, said the study author. Controlled by four study variables - which were antipsychotic medication, duration of the illness, severity of the illness (this, however, only insignificantly correlated to the neuroleptic dosage) and substance abuse - the frontal grey matter decreased partially depending on the dose, and with higher dosages the white matter decreased. However, the lateral ventricles increased in volume. The shrinkage of the grey matter was worst at the beginning of the treatment, the reduction of white matter continued to increase over time. This study showed no significant difference between typical and atypical antipsychotics. Nancy Andreasen and her research team recommend “prescribing these medications in the lowest possible dose to control symptoms. [...] We must also think about how these medications are used for things that have nothing to do with schizophrenia.... they should be used with great care.” – after careful consideration of risks and benefits.
F. Effects of the dopamine receptor blockade
Neuroleptic treatment is essentially a blockade of D2- and other central nervous receptors which can lead to a decrease of so-called positive symptoms. This can improve the symptoms of psychosis. Neuroleptic treatment does not, however, correct the underlying neuronal disorder, but can paradoxically worsen it, especially in the long run, because neuroleptics cause an adverse increase and sensitization of the dopamine receptors as well as a blockade of the pre-synaptic D2-autoreceptors, which leads to a compensatory increase of the dopamine synthesis. These counterproductive effects necessitate increased dosages in the course of the treatment, relapse rates increase up to 3 times due to abrupt withdrawal and symptoms are intensified at later psychoses. A recently published review did not attest to lower relapse rates due to tapering off. Yet the time period for coming off medication was an average four weeks, usually due to the discontinuation of depot preparations. Also, psychotherapy (individual or family) was not offered in any of the studies. This would make a large part of the relapse rate and the revolving door effect drug induced. Excessive dosages and the neglect of psychotherapeutic treatments can lead for the above mentioned reasons to somatic impairment, preventable mental suffering, increased chronification and possibly an increased risk of early mortality.
Furthermore, the neuroleptic induced deficit syndrome or rather negative symptoms do not receive sufficient attention nor are they researched systematically to be included in the benefit-risk considerations. The frequent use of atypicals has not been able to significantly reduce the problem of negative symptoms. Lower dosages are the most important pharmacological strategy here as well.

G. Treatment routine
The current treatment routine is in fact marked by the reduction of resources for mentally ill people. 65 percent of the total expenditure for outpatient psychiatric care goes to psychotherapists treating 25 percent of the patients. Whereas psychiatrists, psychiatric outpatient care clinics (PIA) and neurologists (specializing in psychiatry) treat 75 percent of the cases with approximately 35 percent of the total expenditure. The higher the need for help for mentally ill people the less money meeting the demands is available. A widespread shortfall is a lack of networking associated with lower quality standards as well as frequently limited competency of psychosocial and psychotherapeutic professionals. The main causes for this are the inadequate implementation of the psychiatric personnel regulation (Psych-PV), cross financing in favour of somatic wards and profit transfers by private hospitals. Current payment systems and control mechanism of health insurance funds as well as the one-sided assessment practise fixated on medication by medical services of health insurances (MDK) lead to shortened hospital stays without sufficient and co-ordinated outpatient treatments. There is concern the new financing for hospital treatments, introduced in 2013, might intensify these undesirable developments. Alternatives to
psychiatric inpatient treatments are still not promoted. This does not help the treatment of mentally ill people and often leads to an accelerated “revolving door effect” and is far from shortened hospitalizations in the long run. Excessive dosages and a rising number of prescriptions (polypharmacy) are at times the result of these accelerated hospital discharges. They harm patients and contradict the code of the medical principle “first, do no harm”. The lack of staff in acute care wards is an additional stressful and traumatic experience for many patients.

Team-based outpatient treatments which consider the patients’ overall psychosocial situation (such as in Scandinavia and England) are too seldom put into practice in Germany, because of the strict separation of psychiatric outpatient and inpatient treatment, the lack of therapeutic continuity, the financial incentives for inpatient care and the compensation practices of psychiatrists. At this point treatments frequently narrow down to prescribing psychotropic drugs instead.

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**Studies with dose-related reduction of frontal grey matter without details regarding typical vs. atypical**

Studies with reduction of frontal grey matter – typical > atypical


Studies with reduction of frontal grey matter – FGA ≈ SGA


Study with reduction of frontal grey matter – FGA ≈ SGA after 1 year

Studies without detectable GM-reduction


