Revisiting Whitaker: psychotropic drugs and Mental Health care in Primary Health Care

Revisitando Whitaker: psicofármacos e cuidado em Saúde Mental na Atenção Primária à Saúde

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ABSTRACT Mental Health (MH) issues and the indiscriminate use of psychotropic drugs are a great deal of a problem for the Primary Health Care (PHC) and public health. The aim of this article is to show an updated basis from Robert Whitaker theses in his book 'Anatomy of an epidemic: magic bullets, psychiatric drugs and the astonishing rise of mental illness'. It is presented a synthesis of the book, with specific comments about some topics, aiming for better scientific base of the arguments. The thesis endorses that prescribing psychotropic drugs must be avoided; and, if required, it must be as an acute symptomatic scenario for the least time as possible. The study has positive evidence that a few of these drugs only reduces symptoms, for a short period of time. If chronic used, in a long-term scenario, it seems to actually reduce stability, autonomy and social functionality, leaving the user with serious abstinence from the drug. Specially in PHC (and also in MH specialized services), professionals should have a mindful and discerning approach to psychotropic drugs, and invest in other therapeutic strategies, in order to do something better, less iatrogenic and as effective or more for the mental health patients in the long term.

KEYWORDS Psychotropic drugs. Iatrogenic disease. Mental health assistance. Quaternary prevention.

RESUMO *Os Problemas de Saúde Mental (SM) e o uso indiscriminado de psicofármacos são problemas de grande relevância para a Atenção Primária à Saúde (APS) e a saúde pública. O objetivo deste ensaio é apresentar uma fundamentação atualizada da tese de Robert Whitaker, desenvolvida no livro 'Anatomia de uma epidemia: pílulas mágicas, drogas psiquiátricas e o aumento assombroso da doença mental'. É apresentada uma síntese do livro, acrescida de comentários sobre determinados temas, visando à melhor ancoragem científica dos argumentos. A tese defendida é que se deve evitar prescrever o uso de psicofármacos; e, caso seja iniciado o uso, que seja como sintomático agudo pelo menor tempo possível. Os argumentos giram em torno de que há evidências favoráveis apenas para redução de sintomas, para algumas dessas drogas e para curtos períodos de uso. Com seu uso crônico, há piora em longo prazo quanto à estabilidade, autonomia e funcionalidade social, com problemas graves de abstinência. Especialmente na APS (e também nos serviços especializados em SM), os profissionais deveriam ter uma abordagem mais crítica dos psicotrópicos e investir em outras abordagens terapêuticas, para fazerem algo melhor, menos iatrogênico e tão ou mais eficaz para os pacientes com problemas de SM no longo prazo.*

PALAVRAS-CHAVE *Psicotrópicos. Doença iatrogênica. Assistência à saúde mental. Prevenção quaternária.*

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Introduction

Mental Health Issues (MHI) are highly prevalent and important, especially in Primary Health Care (PHC)[1-3]. PHC, or basic care, can be understood as the network of first-contact health services directly accessible by citizens, which must implement the attributes described by Starlfield[4] – access, completeness, longitudinality, care coordination, family and community approach and cultural competence. It is preferably identified with the Family Health Strategy (ESF), the only Brazilian organizational scheme that offers generalist care to cohorts of territorialized users, and which results have proven to be superior to services without ESF[5]. PHC, in the conception of Alma-Ata[6], also involves political, social, economic and educational actions that are transcendent to the health sector and important for Mental Health (MH), but these dimensions will not be addressed here.

MHI were highlighted by the expansion of the scope of psychiatric diagnoses and the creation of new diagnoses (or subdivision of old ones)[7-10], associated with the progressive mass use of psychotropic drugs[11,12] and the growing medicalization of life's experiences and sufferings[13-16]. This transformed MH care and the use of psychotropic drugs into problems of great relevance for public health and PHC, especially for doctors and Family and Community Medicine (MFC)[17,18].

This problem is connected to the Psychiatric Reform (RP) movement, which trajectory began with the dismantling of asylums and the creation of a network of substitute, territorialized and outpatient services specialized in MH, and only later moved towards PHC. Thus, RP's ideas and assistance proposals only partially entered PHC and MFC.

Despite this gap, PHC is a fundamental locus of the Psychosocial Care Network (RAPS), which was established as a strategy for MH care in the SUS[19]. PHC has great relevance in the care of MHI, the majority of which are treated at this level of care due to its greater reach across territories, because it is the preferred gateway to the SUS and because it is the care coordinator[20-22].

Even in RP discourses, there seems to be an eclecticism that is relatively uncritical of the use of psychotropic drugs, although other therapeutic strategies, generally associated with them, are prioritized. In this regard, in the book 'Anatomy of an Epidemic'[23] and, later, in additions to the work and response to criticism in subsequent publications[24,25], Robert Whitaker argues that the use of psychotropic drugs to treat MHI, despite having, as the type of drug, strong effects of sedating symptoms in the short term and some 'normalization' of behaviors (mitigating social and family tensions that accompany more intense MHI), generates, on the other hand, worsening of long-term evolution in relevant aspects , such as clinical stability, functionality, social reintegration, autonomy, etc.

The aim of this essay is to offer a revisitation of this thesis, which is not anchored in any particular conception of mental health or illness. Methodologically, a free synthesis of Whitaker's book was carried out, following its sequence, with specific comments on selected topics and updating its scientific anchoring. Chapters describing patient experiences are not covered. The main arguments were summarized, with an emphasis on neuroleptics, which hold the greatest belief among professionals and patients, and antidepressants. Schizophrenia and depression were emphasized as they are the extremes of severity and prevalence, respectively. The evidence and arguments for the other MHI covered in the book were not updated, for which a summary of the content of the respective chapters was offered.

The pre-psychotropic context

Chapter 1 describes the enthusiastic psychiatric discourse on the discovery and use of psychotropic drugs, showing the belief and

expectation in the power of these new medications. It was widespread at the time that the use of potent psychotropic drugs, especially chlorpromazine, had revolutionized the treatment of mental illnesses, saving and improving the lives of many people. Its use in psychiatry was compared to the introduction of penicillin in medicine, because, just as penicillin had revolutionized the treatment of bacterial diseases, chlorpromazine had brought an innovative approach to the treatment of psychiatric disorders.

If this were true, it would be expected that the per capita number of people disabled by MHI would have decreased, and then decreased again with the arrival of the second generation of psychotropic drugs (fluoxetine, in 1988). We should have seen a two-step drop in disability rates. However, on the contrary, as the psychopharmacological revolution unfolded, the number of cases of disability due to mental illness in the USA increased sharply, especially after the dissemination of Prozac and other second-generation psychotropic drugs.

In this sense, in the USA and elsewhere, these rates have been increasing progressively. Regarding disability, when only this component is considered in the calculation of disease burden, MHI are responsible for 31% of the years lived with disability[26], whereas, in Brazil, MHI represent 21.5% of all adjusted life years due to disability[1]. Furthermore, MHI are also associated with a poor prognosis of comorbidities and impacts on economic productivity and social and health care costs, with a significant burden on the health and social security systems[1,26-30]. Although recent decades have seen a significant change in pharmacological options, there has been no equivalent increase in recovered cases[31-34].

Chapter 2 narrates stories of psychotropic users, and 3 is dedicated to revisiting the history of chemotherapy in the 20th century and the ideas that guide it, in order to contextualize care in MH and the optimistic, hopeful ideas regarding pharmacotherapy. Since Salvesan, in 1910 (used for syphilis), through animal insulin, in 1922, and penicillin, in 1935, there was nothing equivalent for MHI, only moral and labor treatment in psychiatric hospitalizations. From 1930 to the early 1940s, insulin coma, convulsive therapy and lobotomy were used as treatments in this direction.

In 1946, government funds were directed to MH in the USA, and, in 1949, the NIMH (National Institute of Mental Health) was created, to respond to the consequences of wars and the call for the humanization of asylums. This era, which precedes psychotropics, is one of appreciation and progressive recognition of the importance of MH and an expectation of application of biomedical therapies: MHI would require treatments similar to those of physical illnesses, such as, for example, appendicitis or pneumonia.

The birth of psychotropic drugs

Chapter 4 tells the story of the accidental birth of psychotropic drugs and the association of North American doctors with the pharmaceutical industry, starting in the 1950s. The medicine model (1st – identify the pathophysiology of the disorder; 2nd – develop a treatment that acted against it) was not followed in the development of psychotropic drugs. Phenothiazines were dyes and were studied to be antibiotics/vermicides, without success. Later, one of them proved to be an antihistamine, promethazine, also presenting a tranquilizing and hypnotic effect, relaxing and making surgical patients drowsy. Based on this finding, chemists began studying and developed a more potent derivative, chlorpromazine, which produced effects similar to lobotomy, now in a medicinal way and no longer mechanically.

Recent studies of this psychotropic drug recount the history of psychiatry, from a biological perspective, and its repercussions and developments to this day[9,35]. For example, Caponi36 discusses, from the Foulcautian

framework, the supposed psychopharmacological revolution, its epistemological bases and the associated process of increasing social medicalization, reinforcing Whitaker's arguments in detail.

Then, in England, trying to produce antibiotics, the muscle relaxing effects of a drug derived from a domestic hygiene product, mefesine, were discovered, but with a very short action. From it, meprobomate was developed, which went on the market as an anxiolytic (in today's language) in the USA, under the trade name Miltown. Competing companies soon looked for other 'domesticating' drugs, and chlordiazopoxide (Librium) came onto the market in 1960. At the same time, antibiotics were produced from rocket fuel, and one of its adverse effects gave rise to the first antidepressant (iproniazid).

In parallel, at the same time, an association between doctors and the pharmaceutical industry in the USA starts happening. These begin to control, via prescriptions, access to certain drugs, such as antibiotics and others. When psychotropic drugs arrived, the American Medical Association (AMA) sided with professionals in advertising the new drugs in a highly profitable business for everyone, allowing aggressive marketing in medical publications.

As a result, both the income of doctors increased, doubling in the period from 1950 to 1959, and the revenue of pharmaceutical companies, which exceeded one billion dollars in 1957. At that time, astronomical profits made the pharmaceutical industry a favorite of Wall Street investors.

The news about chlorpromazine was of a miracle drug, and the launch of the first anxiolytic was a success. Due to the influence of psychoanalysis on psychiatrists at the time, in the initial promotion, it was claimed that, despite their effect in leaving patients relaxed and susceptible to treatment, chlorpromazine and Miltown were adjuvants in the psychotherapeutic process and not the treatment for mental illnesses, insofar as the aim was to produce a specific effect through the use of a neuropharmacological element.

However, soon after, this caution was abandoned. After imipramine arrived in 1959, the term 'antidepressant' was born in a renowned newspaper ('Times'). Shortly afterwards, an article by a psychiatrist stated that psychotropic drugs could be compared to insulin, as they acted to neutralize the symptoms of mental disorders, just as insulin neutralizes the symptoms of diabetes[37].

In 1963, the NIMH classified chlorpromazine, based on a six-week study, "as an antischizophrenic in the broadest sense"[38(257)]. The transformation of powerful drugs born almost at random into specific remedies for the supposedly diseased brain chemistry in MHI was complete. Without any scientific basis other than the potent short-term symptomatic effect, there was the conversion of acute symptoms into antipsychotics, anxiolytics and antidepressants.

A supposed basis for biological plausibility came soon after, with the elucidation of the neurochemical physiology of synapses, still in the 1950s; and in the following decade, a mechanism of action for imipramine. In 1965, a theory of chemical imbalance in affective disorders was published, giving explicit birth to biological psychiatry. At the end of the 1960s, psychiatry considered it had made a revolution for good. In 1967, one in three American adults received a prescription for a psychoactive medication[39].

In Chapter 5, Whitaker addresses the hunt for chemical imbalances, which should theoretically and scientifically support the beliefs already in force from the 1960s onwards. His conclusion, however, was that both the hypothesis of depression due to low serotonin and the hypothesis of schizophrenia due to excess dopamine, the foundations of the theory of chemical imbalances, had been shown to be flawed at the end of the 1980s. Likewise, other mental disorders that had been associated with neurochemical problems had neither proof nor sufficient evidence to corroborate this hypothesis.

However, the belief in chemical imbalances persisted. This led researchers on this topic to repeatedly emphasize the same conclusion that the data did not corroborate any of the biochemical theories defended until then[40]. Even so, the unfounded theory was repeated and was once again popularly recognized when Fluoxetine was launched. However, even there, it was clear in the literature that the drugs did not correct the neurochemistry of the brain, but changed it.

Regarding the theory of neurochemical imbalance, studies have corroborated its lack of foundation in empirical data[36,41-50]. Recently, the largest systematic literature review ever carried out on the topic, analyzing publications on the serotonergic theory of depression until 2020, showed that there is no "convincing evidence for a biochemical basis of depression"[51](12). The researchers point out that in the studies analyzed, no evidence of causality or association of depression with lower activities or lower serotonin concentration was found. On the contrary, there appears to be significant evidence that long-term use of antidepressants is related to a reduction in serotonin concentration, which was also corroborated by Pech et al.[52].

The long-term effects of neuroleptics

Chapter 6 goes into long-term clinical outcomes and supports the book's main thesis: psychotropics turn the patients' MHI into chronic conditions. The methodology he tries to follow is straightforward: in the absence of psychotropic drugs and antipsychotic medications, how would patients evolve (recovery rates and social reintegration) over time?

Starting with schizophrenia, the author finds that mental eugenics at the beginning of the 20th century in the USA meant that schizophrenics were hospitalized for life at that time. The fact that schizophrenics never left hospitals was seen as proof that the illness was chronic and irremediable. After World War II, however, eugenics fell into discredit, as it was the philosophy of Nazi society. Social policy changed, and hospital discharge rates soared. As a result, there is a brief interval, between 1946 and 1954, in which we can see how patients newly diagnosed as schizophrenic fared and thus get an idea of the 'natural results' of schizophrenia before the arrival of chlorpromazine. Analyzing data from the time, Whitaker concludes that around 75% of patients hospitalized for a psychotic episode were discharged after a few years and living in the community, before psychotropic drugs; more than half of them did not relapse in subsequent years, and only around 20% needed to remain continuously hospitalized[53-55]. We did not find challenges to these estimates in the most recent literature.

Data from hospitals at the time indicate that the entry of chlorpromazine onto the market in the first decade did not change the discharge percentage any further. What generated massive dehospitalization in the 1960s was a policy change to transfer payments from medicaid and medicare, which, from 1965 onwards, subsidized the hospitalization of mentally ill patients in asylums and community clinics rather than in hospitals – which meant that there was an avalanche of transfers of these patients to this type of clinic.

The intervention studies that began via NIMH (because industries at that time were not required to do so) were designed for 6 weeks of follow-up, and hundreds of them were carried out in the years and decades that followed. Such studies revealed that psychotic symptoms were significantly reduced with chlorpromazine and other neuroleptics. However, regarding long-term effects, the model study was to study the abrupt withdrawal of the drug in user patients and evaluate relapses in 10 months

or one year. The results favored psychotropic drugs, but little was known about the evolution of these patients other than the reduction in short-term symptom scores and relatively short-term relapses[56]. A 2002 editorial in European Psychiatry stated that after fifty years of neuroleptics, there was no convincing evidence regarding the long-term effectiveness of schizophrenia treatments[57].

Whitaker reviews other results from the initial period of chlorpromazine: there is a record of a greater tendency for relapse the higher the dose. This was associated with observational records of the phenomenon of revolving door syndrome: those discharged from hospitalizations taking neuroleptics returned to the emergency room much more often and were readmitted. One study found that the percentage of patients with autonomy five years after discharge fell with the use of neuroleptics. Relapse-free patients in five years fell from 45% to 30%[58]. Three studies funded by the NIMH showed worse long-term results for patients using neuroleptics[59-61]. The author continues to follow several equally convergent studies in the following years, until the beginning of the 21st century. In the last chapter of the book, treatment experiences with no or little use of neuroleptics are visited, concluding that, despite the sedative effects of acute symptoms, this treatment has, in the long term, harmful effects related to its non-use or less use.

Although there is no consensus in the scientific literature regarding the long-term use of neuroleptics, Whitaker's conclusions seem to be corroborated by some recent studies that point to the tendency towards chronicity in their use[62], towards a perception of low cost-effectiveness in the long term[63], as well as a greater risk and accentuation of adverse events, especially with chronic use[63-67], which precipitates discontinuation by some users[67], in contrast to important remission of psychotic symptoms, better recovery rates and better long-term results, especially in functional, cognitive, social and work terms in patients with less or no use of psychotropic drugs[68-79].

The saga of so-called anxiolytics

Chapter 7 deals with benzodiazepines, the first anxiolytics. This is the only category of psychotropic drugs for which there is greater widespread criticism among doctors and the population today. The author summarizes its short-term effectiveness, withdrawal syndrome and various long-term problems.

He points out that, in the short term, these drugs offer relief, improving anxiety symptoms. However, over time, they alter the neurotransmitter system, which triggers compensatory brain adaptations. Consequently, when the medication is withdrawn, there is greater vulnerability to relapses, which can lead to prolonged use, often indefinitely, and the chronification of symptoms.

The author's considerations about benzodiazepines are anchored in recent studies that point to the growing increase in prescriptions for this class of medications and their indiscriminate use, and to the harmful effects of the use of these medications, especially in the long term[80-84] and in the elderly[85-90].

The antidepressants

Chapter 8 deals with depression, also with a historical and narrative review of studies and theories on depression. Again, the author concludes that medications, now much less symptomatically powerful in the short term, have harmful effects in the long term in chronic use.

Whitaker's conclusions about antidepressants are strongly reinforced by studies that indicate that antidepressant use is quite

prevalent and increasing in the long term[91]; that its prolonged use, in addition to having no clinical justification[92], appears to be related to worse results[93-95] and possible iatrogenic effects that increase chronicity and vulnerability to depressive episodes[96-98]. Such studies also frequently show severe withdrawal effects[99-103], and important adverse effects[104], which may impair recovery and increase the risk of readmission[96].

Furthermore, studies with antidepressants versus placebo have demonstrated a high risk of bias and questionable clinical significance[105-108]. Considering the size of the effect, it would be necessary to treat at least 9 patients for 1 to benefit. In other words, 8 patients will be exposed to the adverse effects of these psychotropic drugs without receiving any additional benefit compared to placebo[109,110]. Thus, evidence indicates that antidepressants seem to cause more harm than good, especially in the long term[94,111-113].

Other rare diseases or ones that became common

Chapter 9 deals with bipolar disorder. In a similar way, Whitaker concludes with a table (p. 203), which shows the reduction in good functional and cognitive results from the perspective of long-term improvement in the post-lithium era. Chapter 10 discusses the Gestalt shift that causes us to see only increasingly serious and lifelong illnesses with increasingly earlier onsets in early childhood, instead of perceiving long-term iatrogenic effects from the use of successive psychotropic drugs that are increasingly more easily prescribed. Chapter 11 will deal with the epidemic of psychiatric disorders in children, starting with ADHD, which unfolds into childhood bipolarity, whose diagnosis and treatment figures grow and worsen the statistics of sequelae and long-term functionality. Chapter 12 deals with adolescents, which, now in the post-psychotropic era, can have all the MHI of adults and children, and more chronically the sooner they enter psychopharmacological medicalization.

The construction of an ideology

Chapters 13 and 14 analyze the social, ideological and political-economic trajectory of North American psychiatry. The chapters show their adherence to the option for advertising and propaganda of an ideology that does not resist scientific and historical questioning, but has been victorious in society, science and the psychiatric corporation, with the support of the US NIMH, in association with the pharmaceutical industry and with a systematic concealment of results that, especially in the long term, contradict the propaganda. Chapter 15 talks about profits, the industry's association with user associations and professionals and the astronomical figures of this market.

These chapters shed light on the history constructed by psychiatry in order to maintain the social illusion of the solid benefits of psychopharmacological treatment. To this end, we intentionally and consciously chose to overestimate the positive results and hide the precariousness of long-term results, in addition to silencing critics. The fact that psychiatry has resorted to this method of narrative creation is indicative of demerit, far exceeding the impact that any individual study could have had.

These chapters are still very current. Recent studies reinforce results presented in the book and raise doubts about the integrity of psychiatric scientific literature and its impact on medical practice. They have shown, in addition to methodological flaws and biases of various natures, evidence of planning and selectivity in the execution and publication of results of clinical trials with psychotropic drugs[114-119], including the complicity of some medical journals in "failing to meet the standards of science and peer review"[120(993)], use of spin strategies

(advertising strategies that mislead readers in evaluating the safety or beneficial effects of experimental interventions presented)[121], concealment and recoding of adverse events, among others[64,112], pointing to a low to moderate certainty of evidence[110]. There is strong evidence of overestimation of the effectiveness of psychotropic drugs and underestimation of the associated harm[94,105,112,117].

Furthermore, recent research reiterates the conflict of interests present in studies on the use and effectiveness of psychotropic drugs financed by the pharmaceutical industry, as well as its biased role and that of psychiatry in this scenario[36,41,49,105,112,116,119,120,122-124].

Finally, Chapter 16 comments on alternative care experiences in MH and their best results. Among them, we highlight the Open Dialogue (OD) methodology. Developed and applied in Finland, it presents the best indicators of long-term evolution in the world, with a minimum of temporary use of psychotropic drugs and a lot of support and social mediation, care, dialogue and psychological approaches. The good results of OD continue to be observed in longitudinal studies and literature reviews[65,79,125-129], revealing that it can largely deviate from psychotropic drugs with better results.

Although an extensive critical analysis of Whitaker's book is not within the scope of this article, it is worth mentioning that one of the limits of the book is that it does not address the epistemological fragility of psychiatric diagnoses, which have undergone major transformations in the psychopharmacological era, the object of analysis and criticism that point out its epistemological and social problems[130-132]. Perhaps one of the culminations of these criticisms was the proposal, by English psychiatrists, of a 'drug-centered psychiatry' (instead of a psychiatry centered on diseases or disorders), which dispenses with psychiatric nosological categories by noting that the use of psychotropic drugs do not treat diseases or disorders, although it may have symptomatic effects that may justify its use (preferably, to be avoided), always temporary and with major short- and especially long-term adverse effects, in addition to excessive medicalization of MHI[42,113,133,134].

Final considerations

From Whitaker's thesis, which is increasingly strengthened, the generic clinical guideline of emphatically avoiding the use of psychotropic drugs can be deduced. If this use is initiated, it should be as acute symptomatic for the shortest possible time, without prolongation, with chronic use being actively avoided, for whatever the psychotropic drugs and whatever the MH. It is based on the social and scientific history of psychiatry, especially North American psychiatry, as well as available scientific evidence of various types.

The central argument of the thesis is that psychotropic drugs, in addition to not treating or controlling MHI, when they are effective, only have sedative symptomatic effects in the short term and are iatrogenic in the long term, which other researchers also recognize[93-98,108,111,135,136]. Therefore, given relatively successful experiences of care that do without these drugs, they would be practically unnecessary for MH care, being considered dangerous symptoms and avoided due to their iatrogenesis and chronic medicalization. A corollary of this is that, instead of being considered first-line therapy, psychotropic drugs should be treated as end-of-line, precarious and iatrogenic therapy. A perspective very distant from that currently most present in psychiatry, medicine in general and MFC.

If there is truth to this thesis, and considering the evidence presented, it seems that MFC and other doctors in PHC and other environments need to review their adherence to the use of psychotropic drugs, facing the challenge of recognizing that the guideline for a better clinical result, including in the long term, is a therapeutic eclecticism in which psychotropic drugs will be the last choice, for temporary, brief and undesirable use.

The great difficulty of facing this challenge in the current Brazilian reality should not obscure its institutional, clinical, scientific and ethical importance. From a macro-management perspective of the SUS, this indicates the need for a special and coordinated effort between federal and state managers of PHC and MH (and also higher education and social assistance), to create the conditions for assistance and competencies in specialized professionals and services in MH and (especially) in PHC (intimately articulating them), so that non-psychopharmacological MH care is increasingly available, involving patients, their families and networks of social and community relationships, in a perspective of individual and collective empowerment, human rights, social justice, reduction of inequities and strengthening, capillarization and better qualification of RAPS and PHC.

In a micromanagement dimension, each team of PHC professionals, especially those from the ESF, and above all each doctor must develop a more judicious and critical approach to psychotropic drugs, knowing that they can propose better care, less iatrogenic, less medicalizing and as or more effective for their MHI patients. Such teams must be protagonists in the exploration and construction of community, clinical and institutional resources to be used, in partnership with professionals specialized in MH.

Building the institutional (service and professional infrastructure) and educational (graduation, residencies and continuing education) conditions necessary for this change is part of this urgent challenge and needs to be further debated, investigated and experimented.

Collaborators

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