

Research (Global Analysis)

This report examines nicotine use in five countries: the United States, the United Kingdom, India, China, and Japan. It covers public opinion about nicotine in each country, the major players from academia and the commercial world in each country that influence public opinion, and new possibilities for using nicotine without smoking. It also includes a historical background analysis for the two years prior to the report.

This report will be updated quarterly and will emphasize changes and new information.

This section examines pure, nicotine-related, scientific research in peer-reviewed scientific and biomedical journals in seven geographic regions: Asia, Europe, the Middle East, North America, Central and South America, Oceania, and Africa.

	1	2	3	4	5
Asia	Addiction	Mortality	Smoking as a Risk Factor	Withdrawal	Legislation
Europe	Addiction	Withdrawal	Legislation	Mortality	Relapse
Middle East	Addiction	Withdrawal	Neuroprotective Properties	Side Effects	Mortality
North America	Addiction	Withdrawal	Legislation	Relapse	Mortality
Central & South America	Addiction	Relapse	Withdrawal	Mortality	Legislation
Oceania	Addiction	Legislation	Effects on Pregnancy	Mortality	Withdrawal
Africa	Addiction	Mortality	Effects on Pregnancy	Weight Loss	Withdrawal

Table 3: The top five research topics across geographical regions

We examined the volume of published papers per topic and the institutions the papers came from. Addiction had three times the number of research papers and more funding than any other topic (Figures 7 and 8).

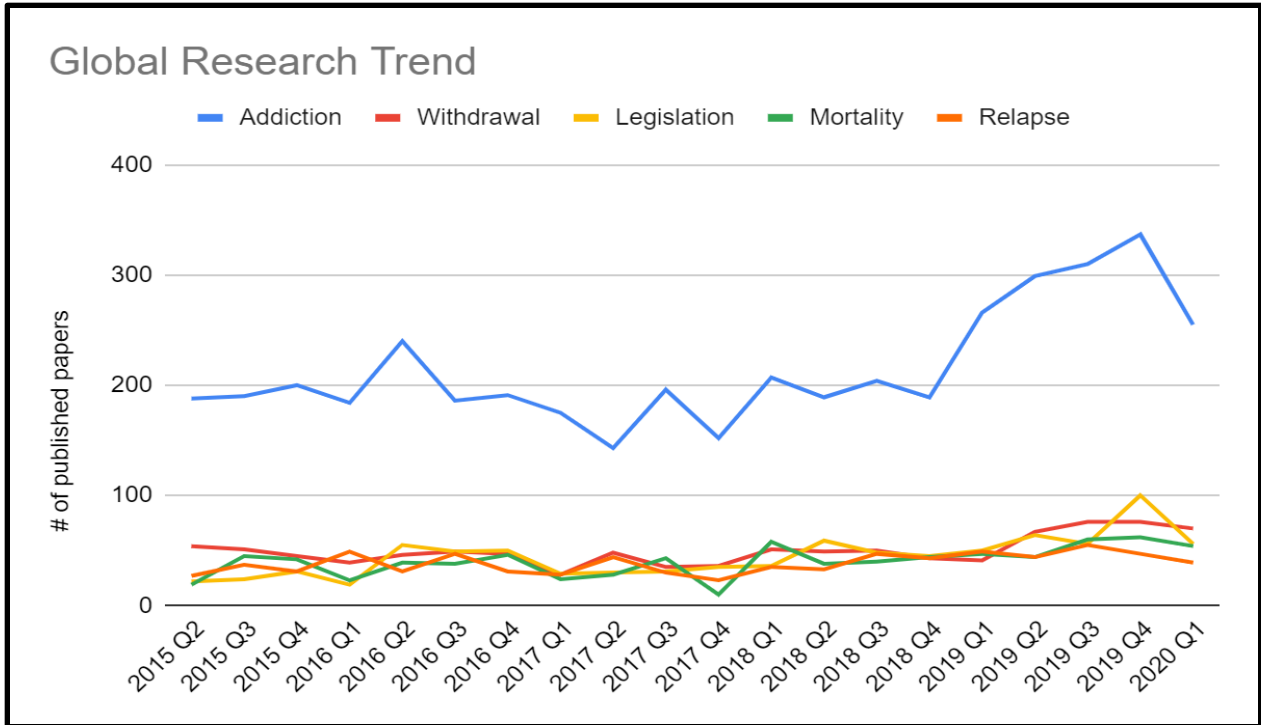


Figure 7: Volume of worldwide published research papers for the top five nicotine-related research topics.

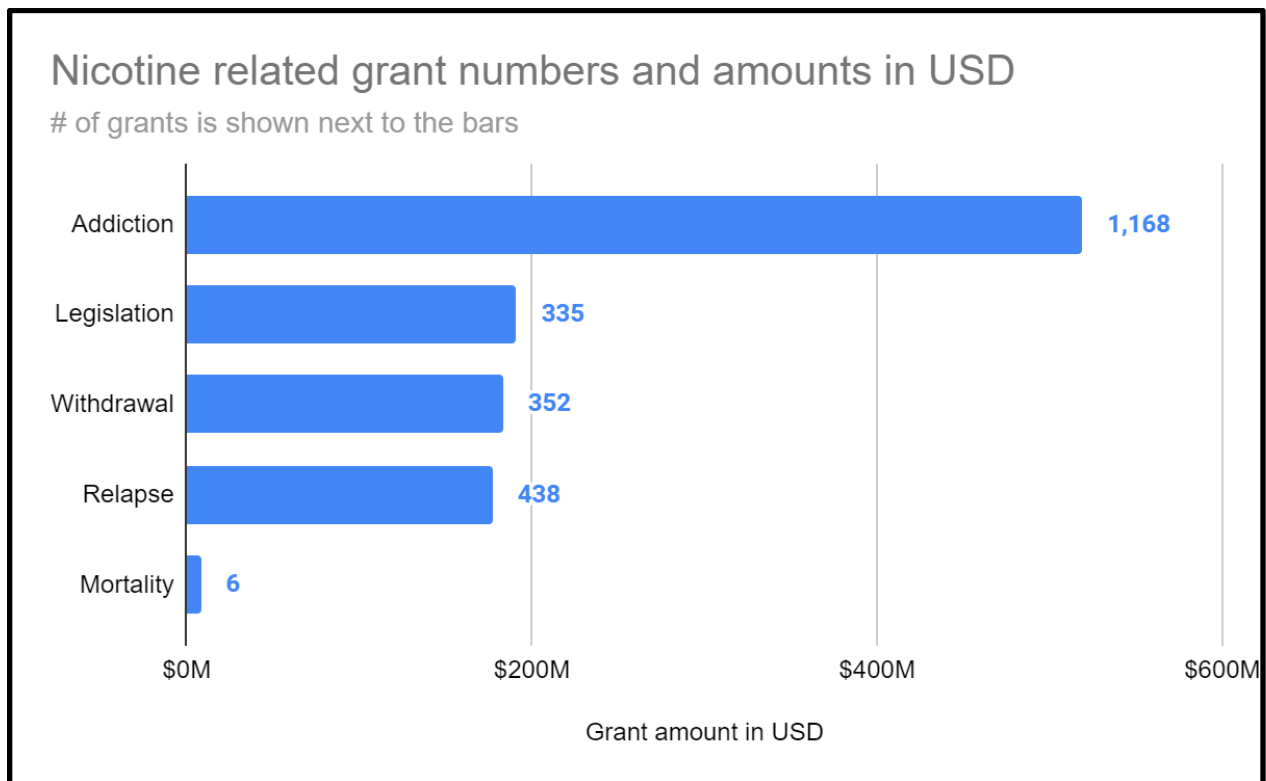


Figure 8: Grant awards and amounts for the leading nicotine-related research topics

	Addiction	Withdrawal	Mortality	Legislation	Relapse
1	Yale University	University of Minnesota	University of Washington	University of Queensland (UQ)	NIH
2	University of Pennsylvania	Virginia Commonwealth University	Yale University	University of California, San Francisco (UCSF)	University of Pennsylvania
3	Virginia Commonwealth University	University of Pennsylvania	University of Minnesota	Johns Hopkins University	University of Florida
4	University of California, San Francisco (UCSF)	University of Vermont	Johns Hopkins University	University of Pittsburgh	Yale University
5	University of Minnesota	NIH	Medical University of South Carolina (MUSC)	University of Vermont	University of California, San Francisco (UCSF)

Table 4: Leading nicotine-related research institutions

Interestingly, the nicotine research field is almost completely governed by academic institutions in the USA. The University of Queensland in Australia is the only non-US institution, and the NIH is the only non-academic institution in Table 4. Sometimes researchers are involved in several related fields, and sometimes research centers within an institution combine their efforts.

Nicotine research primarily focuses on the drug’s harmful aspects, which may be due to their high funding potential and/or the value of potential treatments. Much less research and funding are invested in the connections between nicotine and other medical conditions or nicotine’s positive possibilities (Figure 9).

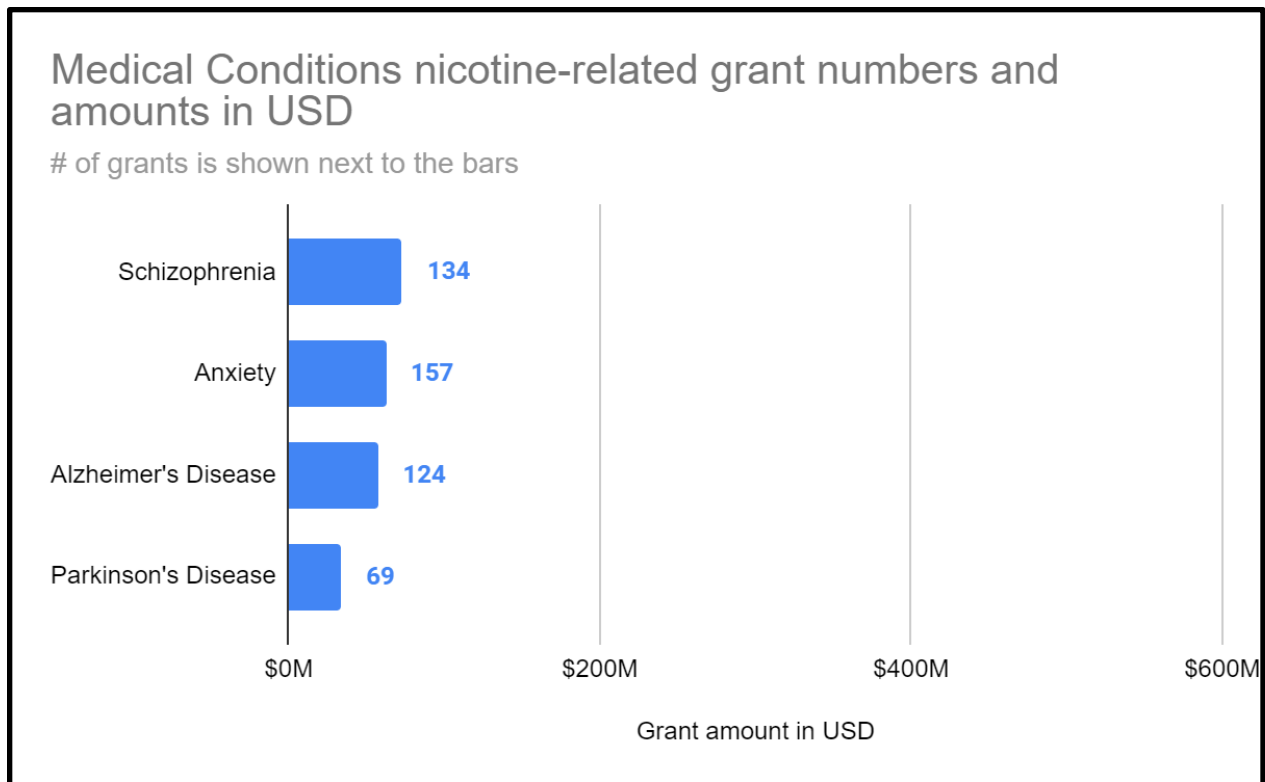


Figure 9: Grant awards and amounts for research on the effect of nicotine on medical conditions

Schizophrenia

Schizophrenia patients experience growing cognitive and sensory deficits, causing them to interpret reality in an abnormal way. The number of schizophrenics who smoke is nearly three times higher than the number of smokers in the general population. Smoking and nicotine consumption reduce the symptoms of the disease and sometimes normalize patients' sensory deficits.

A quick, high level of nicotine is required to produce these symptom-modulating effects. Gum, inhalers, or electronic cigarettes were efficient, while patches, which release nicotine into the bloodstream slowly, were either less effective or not effective at all (1).

Researchers are trying to find a way to deliver symptom-relieving nicotine to schizophrenics without using cigarettes. Nicotine replacement therapies (NRTs) are most successful in patients taking atypical antipsychotic drugs that do not cause extreme adverse side effects. Clozapine, asenapine, olanzapine, quetiapine, paliperidone, risperidone, sertindole, ziprasidone, zotepine, and aripiprazole are some of the most frequently used atypical antipsychotics (2).

Anxiety

Anxiety disorders are characterized by elevated levels of stress hormones and varying feelings of fear.

The effect of nicotine on anxiety disorders is not consistent because, while activating nicotine receptors produces pleasure and lowers the secretion of stress hormones (3), these effects do not last long (4) and are followed by withdrawal symptoms and cravings that increase anxiety (5).

NRTs for smoking cessation may cause severe withdrawal symptoms in smokers with anxiety disorders (6). Researchers are trying to understand the way these therapies act in the body and find treatments that produce fewer side effects (7-9).

Alzheimer's Disease

Alzheimer's Disease is the most common neurodegenerative disease in human beings and is characterized by deteriorating memory, cognition, and social skills (10). As the disease progresses, patients become unable to perform the activities of daily living and require constant assistance and supervision.

There are opposite opinions in the scientific community about the effects of smoking and nicotine on this disease. One group claims that smoking increases the risk of developing Alzheimer's disease (11), while the other argues that smoking keeps it from developing (12).

One aspect of the disease is the loss of brain cells that produce the neurotransmitter acetylcholine (ACh). Nicotine has a similar chemical structure to ACh and binds to the same receptors. In people without Alzheimer's this does not produce much of an effect, but people who have the disease benefit from any kind of ACh receptor activation (especially of the $\alpha 7$ nACh receptor), and this activation improves cognition, particularly in the early stages of the disease (13,14).

Parkinson's Disease

Parkinson's disease is caused by the death of brain cells that produce the neurotransmitter dopamine. Nicotine stimulates dopamine secretion, and scientists are trying to find ways to use nicotine to decrease Parkinson's symptoms and slow the progression of the disease.

Recent findings indicate that nicotine protects brain cells from stress that might cause them to deteriorate (15). While nicotine patches do not slow the clinical progression of Parkinson's (16), consuming nicotine through diet (17) or by chewing tobacco (18) has been shown to reduce the incidence of Parkinson's disease; but once the disease has developed,

even nicotine patches do not slow Parkinson's clinical progression (19) because the damage to nerve cells is irreversible.

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