Antidepressants for Economists and Business-School Researchers: An Introduction and Review

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Antidepressiva sind heute ein wichtiger moderner Massenartikel. Deren wachsende Bedeutung ist jedoch in der Forschung im Bereich der Ökonomik und des Managements weitgehend ignoriert worden. Wir geben einen Überblick über die (wenige) Literatur zu diesem Thema in den Sozialwissenschaften. Wir schlagen vor, Antidepressiva als eine neue Form des Konsums zu modellieren, die im grauen Feld zwischen Medikamenten und Konsumgütern anzusiedeln ist.

The antidepressant pill is an important modern commodity. Yet its growing role in the world has been largely ignored by researchers in economics departments and business schools. Scholars may be unaware how many citizens and employees now take these pills. Here we review some of the social-science literature on the topic. We discuss research on the impact of advertising upon antidepressant consumption, the link between antidepressants and the human 'midlife crisis', and evidence on how antidepressants are connected to crime, suicide, and financial hardship. We argue that antidepressants will eventually have to be modelled as a new form of consumption that lies in the currently grey area between medicines and consumer goods. This topic demands scholarly and societal attention.

Lebenszufriedenheit, Depression, Medikamente, Glück.

Well-being, depression, medications, happiness.

> *Money can't buy you happiness but it does bring you a more pleasant form of misery. – Spike Milligan, British comedian.*
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> *Imagine a society that subjects people to conditions that make them terribly unhappy then gives them drugs to take away their unhappiness. Science fiction? It is already happening...in our own society. Instead of removing the conditions that make people depressed, modern society gives them antidepressant drugs. Theodore Kaczynski, American mathematician and domestic terrorist (the 'Unabomber')*

Sometimes it is said that money cannot buy happiness. What is rarely mentioned in such discussions, however, is that there exists a modern substance that is bought specifically to reduce unhappiness: antidepressant pills. It may not be widely known among social scientists, but antidepressants are becoming a major part of life in the modern world. If you are an economist interested in what is happening in the economy, or a professional manager interested in what is going on in your workplace, you may wish to know that

(i) approximately 10% of the citizens and workers that you meet have probably recently taken an antidepressant pill;
(ii) the scale of antidepressant use in society is rising at a remarkable pace, and, on current trends, may double over the next decade.

In this paper we discuss some of the modern social-science research on antidepressants. Such research is, in principle, complementary to a flourishing line of empirical work on the topic of happiness (including Easterlin 1974, Frey and Stutzer 2002, Graham 2008, Powdthavee 2010, and Van Praag and Ferrer-I-Carbonell 2004).

It is useful to begin by laying out the scale of the issue. Using Eurobarometer data, Blanchflower and Oswald (2011) found that in Europe, in the year 2010, approximately 8% of citizens said they took an antidepressant in the previous year. Within the United States (Kantor et al. 2015), the modern rate of consumption of antidepressants is even larger, at more than 10% of citizens per year. The speed of increase through time is particularly striking, so Blanchflower and Oswald's numbers are likely already to be out of date. According to OECD data, consumption of antidepressant pills in the OECD area doubled over the most recent decade (OECD Health at a Glance 2015, page 185, Table 10.11). In the United States, antidepressant pills are now the third-most prescribed medicine (according to the Centres for Disease Control, 2016). Knapp et al. (2007) is another and earlier review of such numbers; the authors found that antidepressant consumption almost doubled (their Table 7.5 on p. 154) in the ten years they examined, which was the period from 1990 to 2000. Complementary results for earlier data are in Ohayon and Lader (2002), Bauer et al. (2008), Colman et al. (2006), and Olfson and Marcus (2009), and Pagura et al. (2011). Paykel (2006) and Offer (2007) provides interesting background. It seems likely that -- assuming extrapolation is currently a reasonable approach -- the consumption of antidepressants will continue to grow fast in the decade to come.

This paper discusses recent writings on what might be termed the economics and social science of antidepressants. The conceptual issues have largely been ignored by mainstream economists and management scientists. For example, at the time of writing, a Web of Science search on the word "antidepressants" in the American Economic Review, Economic Journal, Academy of Management Journal and Journal of Management Studies finds a total of zero articles. The same kind of search on the Journal of Health Economics produces a total of 7 articles, but most of those papers do not study the consequences of antidepressants (they typically use antidepressant consumption as just one of the possible measures of mental problems in a nation). Moreover, despite the potential implications of antidepressant consumption for corporations and human resource managers, a Web of Science search on the combined terms "antidepressants AND employees" does not produce a single entry in any management or business journal.

Antidepressants are drugs that reduce symptoms of depression (O'Brien et al. 1995 is a formal study of the willingness-to-pay to alleviate different symptoms). They began to be developed in the 1950s and 60s. Since then, antidepressants have become more and more widely used in the industrialized world. Today, many people take substances such as Prozac (fluoxetine), and that word itself has become familiar to most citizens. Currently, there are five main kinds of antidepressant:

- *SSRIs (Selective Serotonin Reuptake Inhibitors)*
- *SNRIs (Serotonin and Noradrenaline Reuptake Inhibitors)*

- *NASSAs (Noradrenaline and Specific Serotoninergic Antidepressants)*
- *Tricyclics*
- *MAOIs (Monoamine oxidase inhibitors)*

The biochemistry of these substances is still not entirely understood. However, SSRIs, the most common kind of antidepressants, act in a way that raises serotonin in the human brain. Serotonin is a form of chemical 'messenger' involved in the communication of internal brain signals. As the acronym implies, an SSRI slows the rate at which serotonin is reabsorbed, which, loosely, allows a greater quantity of serotonin to be left available. Hence an SSRI could be thought of as acting like a partial plug in a bath of water – allowing the bath to stay fuller for a longer period.

In the past three decades, there has been a rise in the consumption of these antidepressants. For the United Kingdom, for example, the latest government figures (NHS Digital, 2017) show that between 2015 and 2016 the number of prescriptions for antidepressants rose 6% in a single year, from approximately 61 million in the UK in 2015 to nearly 65 million in 2016. The UK government report notes that this was the largest single growth rate for any kind of prescription medication. The rate of prescribing has doubled in a decade. The number of UK antidepressant prescriptions was approximately 31 million in the year 2006. The underlying reasons behind their international increase have yet to be disentangled by empirical and theoretical studies. Has depression become more prevalent in the late 20th century? Have people become more aware of the symptoms, while the stigma of mental health problems has been diminished, which would lead to more patients seeking medical help? Or has it been due to the technical change and advancement in antidepressant medications and in-patient treatment with fewer side effects and doctors prescribing antidepressants more freely?

In this paper we put forward the view that antidepressants are unlike traditional commodities. What distinguishes them from, say, apples or motor vehicles or shoes is that they are taken predominantly by unhappy, unwell, and occasionally potentially irrational agents, which may need to be accounted for in modelling of the decision-making process. Little thought by economists has been put into how, analytically, that modelling might be done. Moreover, the decision to take antidepressants is, in a sense, influenced jointly by two agents simultaneously -- both the patient and the doctor. Both have to agree on whether the medication will be consumed by the patient, and which class and brand would be suitable. This decision is later subject to revisions, because patients are heterogenous in what is the appropriate medication. Side effects, and treatment effectiveness, of different medications also vary from patient to patient. Finally, antidepressants are usually not seen as desirable long-term consumption goods. Instead, they are often designed as commodities to smooth out consumers' levels of wellbeing across temporary bad times. The roles of sociological influence and sheer norms of behavior are, as might be guessed, also apparently important factors is shaping how often antidepressants are prescribed (Sleath and Shih 2003).

Later sections of the paper also review the possible effects of advertising upon antidepressant consumption, the connections between antidepressants and the 'midlife crisis', and recent research on how antidepressants are linked to crime, suicide, and financial hardship. We conclude that antidepressants will eventually have to be modelled as a new form of consumption.

Background and Overview

Moncrieff (2008) is a valuable study of the history of antidepressant use. Newman and Hassan (1999) examine use among elderly people; the authors calculate, for that era, that approximately 4% of the population were taking antidepressants.

Using Eurobarometer data from the year 2010, Blanchflower and Oswald (2016) show that, after adjusting for other characteristics, the probability of taking an antidepressant is greatest among those middle-aged, female, unemployed, poorly educated, and divorced or separated. A strong hill-shaped age pattern is found -- for males and females and in Western and Eastern Europe -- that peaks in people's late 40s. Its shape seems similar across different sub-samples of people.

This hill-shaped finding is potentially an important one for management scientists and economists. First, a hump-shape in antidepressant consumption is consistent with a famous pattern from the broader 'happiness' literature in social science. Many researchers have argued -- though a few scholars remain unconvinced -- that there is evidence of a midlife low in human beings. A U-shape in happiness through the lifespan has been found in large samples of citizens across dozens of nations (Frey and Stutzer 2002, Blanchflower and Oswald 2008), and an equivalent pattern has also been shown in one study of chimpanzees and orangutans (Weiss et al. 2012). Second, the idea that people of this middle-age group have low psychological well-being has potential ramifications for business corporations. Senior leadership positions are traditionally allocated to people as they reach their 50s. Yet little attention has been paid by scholars to the questions: (i) how are leadership selections affected by the turmoil of the 'midlife crisis' that many humans apparently endure, and (ii) might this be an unreliable part of life for the choice of long-term leaders?

Antidepressants and direct-to-consumer advertising

Prescription drugs are mostly marketed via three channels: medical journals, physician detailing, and direct-to-consumer advertising (DTCA). Direct-to-consumer advertising started in the United States in the 1980s, and has been subject to regulations by the Food and Drug Administration (FDA). These restrictions were relaxed in 1997 and, together with New Zealand, the U.S. is now one of the few industrialized countries that allows full direct-to-consumer advertising of prescription medicines. Potentially as a result of the changes in FDA regulations, DTCA spending increased by 300% between 1997 and 2005, compared to a 90% increase in advertising aimed at doctors.

One of the important questions about the impact of DTCA is that of whether it expands the market for the advertised product or leads to an increase in the entire pharmaceutical-class sales (or both). While attempts have been made to answer this question for broader groups of pharmaceutical products, Donohue and Berndt (2004) add to the literature by attempting to answer this question for antidepressants. Their study investigates the impact of DTCA and physician detailing on the choice of antidepressant drugs on individual level. The main hypothesis is that antidepressants with higher DTCA spending are more likely to be prescribed. However, the probability of choosing the drug should also decrease with the prescription co-payments. In addition, because antidepressants are experience goods, a drug is expected to be more likely to be prescribed the longer it has been on the market because consumers and physicians are more familiar with it. The study focuses on three classes of antidepressants: selective serotonin reuptake inhibitors (SSRIs), serotonin nore-

pinephrine reuptake inhibitors (SNRIs), and serotonin antagonist and reuptake inhibitors (SARIs). The analysis is based on the assumption that the choice of medication is influenced by the characteristics of the person choosing the medication, the features of the medication, as well as the doctor's preferences.

Individual-level data are preferable for such a study, because such data make it possible to account for patient characteristics that lead to different treatment choices, and to keep track of out-of-pocket spending on medications. Moreover, such a data set also allows researchers to treat aggregate DTCA expenditure as exogenous to the choice of antidepressants. The data used for the authors' analysis consists of health-insurance claims for the use of medical services and prescription drugs, marketing data on pharmaceutical promotion, and the characteristics of the medications. Their sample is limited to the first prescription for each patient between 1st July 1997 and 31st December 2000. Individuals with missing data on insurance coverage were excluded from the sample. The final sample consisted of 25,716 individuals, 15% of whom were diagnosed with depression and over 65% of whom were women.

A nested logit model was chosen by the authors for the baseline specification, with main explanatory variables being monthly spending on DTCA and monthly spending on physician detailing for each of the considered medications. One limitation stems from the fact that it is impossible to estimate the individual-level exposure to advertising and physician detailing because aggregate-level promotional data are used.

Donohue and Berndt's (2004) main conclusion is that DTCA spending does not seem to have a significant impact on antidepressant choice. A 1 standard deviation increase in DTCA spending (approximately $43,816) was associated with a 0.5% increase in probability of the antidepressants being chosen, but this result was not statistically significant. While DTCA had no effect on patients diagnosed with the Major Depressive Disorder, the effect was positive for those with anxiety disorders. However, a 1 standard deviation increase in spending on physician detailing ($1,400) was associated with a 10-15% increase in the probability of choosing an antidepressant. Moreover, in agreement with the initial hypothesis, a 1 standard deviation increase in FDA indications was associated with 10-15% increase in the probability of an antidepressant being chosen. Interestingly, the probability of choosing an antidepressant rose after an FDA approval for its off-label use. The probability of choosing a medication rose by 12-18% with every 3 years of its presence on the market. The results were robust to including product-specific fixed effects. The main implication of the authors' paper is that DTCA appears to affect whether someone receives a medication, but not which antidepressant they receive.

A paper by Avery, Eisenberg and Simon (2012) improves upon previous research by connecting the levels of direct-to-consumer advertising in television and magazines to individual-level media consumption. Their data are aggregated at annual level. The individual-level demographic characteristics data, as well as information on whether the respondents used antidepressants during the past 12 months, their severity of depression and media utilization, were drawn from the 13 waves (2001-2007) of the Simmons National Consumer Survey (2008). Other data used included information on advertisements aired on TV between 2001 and 2007 (Kantar/TNS Media Intelligence) and magazine DTCA (sourced from a digital pharmaceutical advertising database, PhADS, archived at Cornell University). The final sample included 146,775 individuals for magazine advertising and 106,865 individuals for TV advertising. Female respondents constituted 56% of the sam-

ple, and the prevalence of depression was higher in this group. To measure the potential exposure to DTCA, the authors linked data on reported magazine reading and television viewing behaviour to data on antidepressant advertising during television programs and in magazines that the respondents reported watching/reading.

The authors' baseline specification is a logit model, with the probability of taking an antidepressant as the key variable. It is assumed to depend on TV/magazine antidepressant advertising exposure, a vector of individual-level factors, TV/magazine fixed effects, and TV watching or magazine reading intensity. The authors' models are estimated separately for TV, magazines, and both. The marginal effects of the DTCA exposure variables are interpreted as the causal impact of exposure to different levels of antidepressant advertising on the antidepressant utilization among individuals suffering from depression – 60% of depressed individuals reported taking antidepressants. Exposure to high or low levels of advertising (defined as above or below the average) led to an estimated 3 or 10 percentage point increase in the probability of taking an antidepressant, respectively. The effect was found to be non-linear, with higher prevalence among women (it was statistically significant for both TV and magazines, while it was only significant for TV advertising among men). These effects were more concentrated among those with more severe depression symptoms. No evidence for an interactive effect of exposure to both TV and magazine advertising was found.

Avery and colleagues note a number of difficulties. First, the use of annual data made it necessary to work with the assumption of constant media utilization throughout the year. Second, it was impossible to examine the impact of DTCA on off-label use of antidepressants.

To address the question of market response, Meyerhoefer and Zuvekas (2008) investigate the shape of the demand curve for antidepressants and its implications for direct-to-consumer advertising in this class of medications. The theoretical model underlying their study incorporates costs that influence the consumption of medical care – including out-of-pocket medication costs borne by patients, insurance premiums and the costs of in-patient treatment. Consumers are assumed to have preferences over their health status and other consumption goods. The class of newer antidepressants is treated as a single good, while health is taken to be a stock variable that depreciates over time (the rate of depreciation depends on the intensity of healthcare utilization). The analysis encompasses the period between 1996 and 2003, and the quarterly data for new antidepressants DTCA are merged over 100 markets. Only individuals with private insurance coverage for at least 5 quarters during a two-year period are included in the sample. The final sample consists of 417,400 person-quarter observations (the entire insured population), of which 29,896 were for the consumers who used antidepressants.

In the study, the effect of direct-to-consumer advertising is captured by exploiting the variation in DTCA spending over time and regional market-level variation in DTCA. The baseline specification is a correlated random-effects model with the number of antidepressant prescription fills per person in a quarter as the dependent variable. 13% of all antidepressant prescriptions were generic. Two models are estimated in order to separate the case of an initiation of treatment (a probit model of any antidepressant use in the entire population) and the case of treatment adherence (an ordered probit model for the number of prescription fills for the population of insured individuals who used antidepressants over a two-year period).

To go some way to resolve the potential issue of endogeneity, a fixed effects estimator is included – there was no effect on the estimated coefficient. Additional variables were also included to model potential endogeneity of end-of-year prices of antidepressants. The results show that higher levels of DTCA increase the likelihood of any use of antidepressants and the number of prescription fills among those who already use antidepressants – the demand curve rotates anti-clockwise and shifts outwards. Doubling the per-capita spending on antidepressant DTCA is associated with a 5% increase in the likelihood that a consumer uses antidepressants, while doubling of the expected price of antidepressants reduces this likelihood by 15%. However, higher levels of DTCA spending may have a negative effect on the number of prescriptions filled (the price elasticity is near zero at $100 per fill). If patients expect to receive free drugs, a 20% increase in DTCA leads to a 10% increase in the number of filled prescriptions. If they expect to pay $10 per fill, this effect decreases to 0.8%. Finally, the results suggest that the task of matching patients to appropriate medications is best left to the doctors.

Antidepressants and suicide

Selective serotonin reuptake inhibitors (SSRIs), introduced in the 1980s, were a new class of antidepressants that changed the treatment for depression. Because of their good tolerability, their general lack of severe side-effects, and the fact that they are moderately safe in overdose, SSRIs quickly became the most frequently prescribed class of antidepressants. Some of the SSRIs became widely used in treatment disorders other than the Major Depressive Disorder – obsessive-compulsive disorder and anxiety disorders, among others. Nevertheless, there is a caveat. In the initial stage of treatment with SSRIs, patients may experience increased energy levels before any improvement in mood levels – these concerns originated from results from randomized control trials (RCTs). As a result, a depressed patient with suicidal thoughts may become more likely to realise his/her intentions. Children and adolescents were thought to be most likely to be affected by this side effect. The growing controversy about the effect of SSRIs resulted in the FDA issuing a law in 2004 requiring a black box warning on all SSRI products informing about the higher probability of suicidal thoughts among children and adolescents in the early stages of therapy.

The results from RCTs were put into doubt due to the nature of an event such as a suicide. Because of the small sample size in such experiments, it is difficult to detect any policy-relevant effects. Some non-experimental studies tried to address these concerns, but issues with the endogeneity of SSRI utilization rates emerged.

Markovitz and Cuellar (2007) investigate the relationship between antidepressants and suicide among younger patients in the 10-14 and 15-19 age groups in the United States for the period between 1997 and 2003. The central question of the paper is whether antidepressants are associated with suicide, and if so, how. Suicides in an age group for a given state and quarter are assumed to be a function of antidepressant prescriptions, determinants of suicide other than antidepressants, quarter-year effects, state fixed effects and an interaction term between time and state fixed effects. Because of potential endogeneity issues, the estimates from this specification should not have a causal interpretation. In particular, potential reverse-causality between antidepressants and suicide and unobserved factors in the error term may be problematic. Data on completed suicides were taken from the Multiple Cause of Death files from the Center for Disease Control, while information

on antidepressant prescriptions was taken from the IMS Health National Disease and Therapeutic Index (NDTI). NDTI data have two limitations; first, the numbers include only antidepressant prescriptions issued by office-based physicians (and no prescriptions from in-patient facilities). Second, it is not possible to confirm whether the prescriptions were filled after the patients received samples during a visit. The number of drug appearances per 1000 patient visits (where a drug appearance is a mention of a drug during the visit) is taken by the authors as a measure of antidepressant use. Actual prescriptions constitute 66-91% of all drug appearances, varying by the drug and year under consideration. Antidepressants in the study are divided into four classes: tricyclics and tetracyclics (TCAs); monoamine oxidase inhibitors (MAOIs); SSRIs/SNRIs, and newer generations of antidepressants (NGAs). There are also two measure of psychiatric coverage in a state: the number of psychiatrists and the number of mental hospital beds per 100,000 of population. Labour market data are also included, because economic conditions can affect the rate of suicide. Among controls in the regression, there are the percentage of state population living in rural areas, religious identity, and state annual per capita beer consumption. Because of the unobserved factors in the error term, and potential reverse-causality between suicide rates and antidepressant prescriptions, the results cannot be viewed as definitively causal.

The authors' estimates results show that among 15-19 year olds, NGAs were negatively associated with suicide. The results became insignificant when linear trends and fixed effects were excluded from the specification. The new therapies for SSRIs/SNRIs and TCAs were not significantly associated with suicide rates. There was no apparent relationship between antidepressants and suicide among the 10-14 age group. Once state fixed- effects and linear trends were included, a high state unemployment rate was positively associated with suicides, while beer consumption was negatively related with suicide.

Ludwig, Marcotte and Norberg (2009) offer one of the most carefully designed estimates of the effect of SSRIs on suicide rates. They collect data on suicide mortality (1980-1999), annual SSRI sales for 26 countries (starting in 1990), dates of drug approval for SSRIs dating back to 1980 and other characteristics for each country (population age distribution, unemployment, real GDP per capita, divorce rates and healthcare expenditures). Population-weighted least squares estimation method is used by the authors, with the natural logarithm of the number of suicides per 100,000 in each country in a given year as the dependent variable. Country-specific time trends were included, with the standard errors clustered at the country level – most variation in suicide mortality occurred across countries rather than across time. To address the issue of potential endogeneity of SSRI sales, an instrumental variable design was preferred to ordinary least squares. Ludwig et al. (2009) used the institutional differences that affect pricing, regulation, distribution and general drug use as an exogenous source of variation. As a proxy for the institutional differences, the authors use variation in SSRI sales as predicted from sales of other (non-psychiatric) drugs that were introduced in the same time period. A further assumption stated that patients in countries with higher rates of new drug diffusion were not less likely to start treatment with SSRIs. The IV estimates demonstrate that an increase of 1 pill per capita in SSRI sales lead to a 5% decrease in suicide mortality (compared to 2.5% from OLS estimates). The effect is the largest for relatively younger individuals. Adding the age structure of society in the OLS specification reduced the magnitude of estimates by one third. In this study, the results were robust to changes in the baseline specification and

to changes to the sample. Firstly, they are not driven by outliers. Restricting the sample to OECD countries only did not change the estimates. Countries with different projections for SSRI sales had similar suicide trends prior to the introduction of SSRIs. There was no significant relationship between predicted SSRI sales growth and healthcare spending or other causes of death (like accidents). Moreover, the consumption patterns for other classes of antidepressants remained relatively stable and there was no systematic increase in use of psychotherapy during the study period. In their concluding remarks, the authors state that SSRIs seem effective in saving lives. Assuming that an antidepressant pill costs $0.11 in the U.S., each additional $22,000 spent on SSRIs could, they argue, prevent one suicide completion.

A recent ecological study by Gusmao et al. (2013) extends the analysis of antidepressants and suicide to Europe. They aim to identify trends in antidepressant use and suicide rates in 29 European countries between 1980 and 2009. Moreover, they investigate whether in any countries an increase in utilization of antidepressants was preceded by a decline in suicide rates. Between 1980 and 2000, the suicide rate fell in most EU15 countries, while in the 1995-2010 period, the suicide rates decreased in all EU27 countries, except for Malta, Poland and Portugal. Previous research, they argue, suggested an inadequacy of randomized control trial studies, the results of which were sometimes contradictory. Moreover, a negative correlation of suicide with economic development and association between higher suicide rates and alcohol consumption, divorce and unemployment had been proposed. The authors explore these as possible forces driving the trends in the suicide rates across countries. The data used by Gusmao et al. are mostly from the World Health Organization. These include the completed suicide rates, population data and national unemployment rates, GDP per capita, as well as per capita alcohol consumption. The divorce rate per thousand was sourced from the OECD Social Indicators. The total antidepressant consumption is defined in terms of the DDDs (Defined Daily Dosage) per 1000 per day. Their final sample consisted of 870 observations for 29 countries across varying time frames. The correlation between suicide rates and antidepressant utilization was examined using a Pearson correlation coefficient. The same method was used to calculated correlations between the suicide rates and the other possible determinants of suicide.

General linear mixed models (GLMM) are used for the authors' main specifications. The authors anticipated that year-of-data observation could have strong explanatory power for the variation in the suicide rates and no year dummies were included in the models. A Poisson regression was used as a robustness check. As SSRIs became widely available in 1994, the data were split into two samples – for the period 1980-1994 and 1995-2009.

Overall, this study found that antidepressant utilization increased by 40.33 DDD per 1000 per day. This growth tendency was continuous, with an annual average growth of 19.83% in DDD/1000/day. This was accompanied by a mean decrease in suicide rates of 0.81%. Only Poland, Spain and Ireland had a higher suicide rate at the end of the study period than at the beginning. In general, in almost all countries an increase in antidepressant utilization was associated with a decrease in the suicide rate. However, in countries where the suicide rates were low to begin with, antidepressant treatment had a smaller impact. The suicide rate was found to be inversely correlated with GDP per capita, except for Poland, Ireland and Spain. No significant correlation patterns were uncovered with respect to alcohol consumption, unemployment and the divorce rate. In the main model, a

one unit increase in DDD/1000/day for antidepressants diminished the suicide rate by 0.088 units, while a unit increase in the divorce rate led to 1.273 unit increase in the suicide rate. Antidepressant consumption had a negative impact on suicide rates in both subsamples, but the effect was more pronounced for the 1980-1994 period.

Antidepressants and behavioural outcomes

One of the common side-effects of taking antidepressants, particularly in the early stages of therapy, is a temporary decrease in cognitive abilities. Nevertheless, is it possible that not taking antidepressants when needed leads to a more significant negative effect on human capital?

A study by Busch, Golberstein and Meara (2011) attempts to answer this question by examining the impact of SSRI safety warnings issued by the FDA in 2004 on academic and behavioural outcomes among 100,000 individuals in the 12-17 age group in the U.S. The issues of the so-called "black box warning" preceded an abrupt increase in the youth suicide rate in 2004 and 2005, and resulted in a 20-30% drop in paediatric use of antidepressants. Moreover, primary care physicians were issuing a smaller number of prescriptions, compared to psychiatrists after the warning. The significant drop in utilization of antidepressants among youths is arguably an appropriate natural experiment to study any undesirable impact of safety warnings. The authors use information on adolescents in Medical Expenditure Panel Surveys (2002-2006) to examine outcomes of individuals seeking treatment before and after the change in regulation, with non-depressed youths serving as the control group. The final sample consists of 116,371 individuals, of which 6.6% were classified as having probable depression (more prevalent among girls). Academic achievement, substance use and delinquency were taken to be measures of academic and behavioural outcomes. Except for binge drinking, substance abuse was half as common among non-depressed individuals. Moreover, grades were reported to be stable among the control group. Individuals with a recent episode of probable depression were 8.6 percentage points (pp) less likely to get a B (or higher) and 3.5 pp less likely to get a C or better after the FDA warning was issued. The effect for girls was, respectively, a 11 and a 6 percentage point decrease. There was no change in the likelihood of obtaining an A.

While there was little effect on binge drinking, these individuals were also 4.6 percentage points more likely to smoke. Girls were more inclined to take illicit (5.4 pp) or non-medical (4.3 pp) drugs. Overall, fighting increased by 6.5 percentage points. Stealing increased by 4.6 percentage points, but this effect occurred only among girls. There was no effect on the likelihood of seeking treatment for depression. The authors note that the results are reduced form estimates and only uncover the short run effect within 1 to 12 months after the issue of safety warnings.

Kuhn, Lalive and Zweimuller (2009) demonstrate that job loss caused by plant closure leads to greater antidepressant consumption. Gunnell et al. (2003) and Markowitz and Cuellar (2007) suggest that, for certain population groups, there is evidence of beneficial effects from antidepressants in reducing the rate of suicide. Innovative research by Askitas and Zimmermann (2011) examines data on the timing of people's Google searches on antidepressants' side-effects.

Ludwig and Marcotte (2005) are concerned about the possibility that selective serotonin re-uptake inhibitors (SSRI) may increase the risk of suicide for at least some patients. Prior randomized trials, they argue, are not informative on the question. Using variation across

countries over time in SSRI sales and suicide, the authors conclude that an increase of one pill per capita (a 13 percent increase over 1999 levels) is associated with a 2.5 percent reduction in suicide rates, a relationship that is more pronounced for adults than for children. They suggest that expanding access to SSRIs may be cost-effective.

Antidepressants and crime

Work by Marcotte and Markovitz (2010) investigates whether the significant decline in crime rates since the early 1990s can in part be explained by the increasing trend in consumption of antidepressants. A simple time series comparison shows that the increase in sales of newer generations of antidepressants was accompanied by a decline in crime rates, while other economic and social factors remained relatively stable. The central hypothesis of their study is that "the diffusion of improved treatment for various mental illnesses in the community reduced underlying behavioural antecedents to crime". The authors exploit U.S. state-level panel data for the period between 1997 and 2004, which includes information on crime and state-level drug diffusion. In the baseline model, the crime rate in a given age group in a given year is assumed to be a function of psychiatric drug prescriptions, other measures of crime as well as time and state effects.

The estimated effect of all psychiatric prescriptions on violent crime was found to be negative, but it was statistically insignificant. There was no association between violent crimes and SSRIs, SNRIs and antipsychotic medications. When common trends across states were accounted for, there seemed to have been a significant effect of NGAs, SSRIs and antidepressants in general on property crime rates. Finally, there was a weak relationship between psychiatric drug prescriptions and homicide. There was no significant relationship between arrests for violent or property crime among any age groups and psychiatric prescriptions.

During the analysis period, the prescriptions of the new generation antidepressants (NGAs) increased by 47%. Building upon this fact, the authors' model would predict a 300,000 reduction in the total number of violent crimes. In reality, violent crimes decreased by 15,000. This would imply that the expansion of mental health treatment explains 5% of the reduction in violent crime rates. The main findings of this paper imply that NGAs and stimulants may be helpful in reducing reported violent crime, while antidepressants are negatively related to homicide among older age groups.

Antidepressants and financial hardship

Lin et al. (2013) make a first step towards establishing the link between financial hardship and the mental health treatment. They focus on the recent housing crisis in the United States, where house prices dropped by as much as 20% between 2006 and 2009.

The study focuses on the 55-64 age group for two reasons. A sharp increase in suicide rates was observed among the near-elderly during the study period. At the same time, this was a group in which home ownership constituted a high proportion of saving. Financial hardship, the authors say, can have two counteracting effect on mental health treatment. First, it may lead to higher stress levels and, in turn, to higher antidepressant use. Second, it may also lower the utilisation of mental health treatment because of an individual's inability to cover associated expenses.

The baseline model in the study links changes in local house prices to changes in the volumes of antidepressant prescription. A differences-in-differences specification is used to control for contemporaneous change in the local level of prescriptions for all drugs other than antidepressants and also for statins (a class of medications used by patients with high cholesterol levels.) The county-by-months data cover prescription drug claims in the United States between December 2004 and December 2009. The data set consists of 505 million prescriptions covering 2961 counties and all states. The prescriptions were claimed in 32 thousand pharmacies and 35 drugs were classified as antidepressants. The house pricing index data was taken from the Freddie Mac House Pricing Index (HPI). In the study, the baseline model links the logarithm the number of filled prescription to the house pricing index and unemployment, while controlling for contemporaneous unemployment. County, month and state-year fixed effects were included. The correlation coefficient between HPI and antidepressant prescription volumes was found to be -0.76. The results from the baseline model indicated that the 20% decline in home prices was associated with a 7.51% rise in the volume of antidepressant prescriptions. This implies that the housing crisis could, in principle, explain a quarter of the observed increase in the use of antidepressants. The authors' difference-in-differences specification showed that the 20% decrease in the HPI was associated with a 4.53% increase in antidepressant prescription claims relative to all other drugs, and a 3.57% increase in antidepressant use, relative to statins.

Antidepressants and Regulation

The last two decades have seen an increase in the development of mental-health therapy and services utilization. But how important are regulation and healthcare management systems in obtaining access to these latest developments? Domino (2012) asks the question of whether the variation in the level of managed care across U.S. states in the period between 1991 and 2005 affected state-level diffusion of newer generations of the whole class of psychotropic medications in fee-for-service Medicaid programs. In 2003, psychotropic medications accounted for 23% of total healthcare expenditures in the United States. The diffusion of new products in this class of medications differed across regions and patient populations. Among possible explanations for the differences in diffusion are differences in social capital, state investment in population, relative wealth and the degree of interactions between prescribers. The main goal of author's study is to understand which factors affect the diffusion of psychotropic drugs in the Medicaid population, because diffusion in this population mimics the diffusion in other populations. Nationwide data from the state Medicaid programs between 1991 and 2005 for three new classes of psychotropic medications are used: selective serotonin reuptake inhibitors (SSRIs introduced in 1980s), selective serotonin-nonrepinephrine reuptake inhibitors (SNRIs, introduced in 1994) and atypical, or second generation, antipsychotics (SGAs, introduced in 1980s). The first two groups are antidepressants. Quarterly data on total prescription in fee-for-services Medicaid programs in 49 states and the District of Columbia were obtained from the Center for Medicare and Medicaid Services (CMS) and the Medical Drug Utilization Files.

The dependent variable for each of the three classes of medications was measured as the percentage of total DDDs (drug units in standard person-day doses) in the entire drug class (antidepressants and antipsychotics) in each quarter. To measure drug use, all medication use was converted into DDDs and then aggregated at state-quarter level. The asso-

ciation between managed care and psychotropic drug diffusion was examined using three different measures of managed care: capitated managed care plans, capitated models and more loosely managed models, and behavioural health carve-outs. The baseline specification was an epidemic model with a fourth order polynomial and state fixed-effects. Managed care was assumed to be exogenously determined, as the author investigated the composition rather than the size of the market for psychotropic drugs. The estimated models also include some state characteristics to control for time-invariant factors. While SSRIs constituted 23% of all antidepressant prescriptions in 1991, as much as 74% of antidepressants use could be attributed to this class in 2005. In the same period, use of SNRIs increased from 3 to 9 percent of all antidepressants. Prescriptions for atypical antipsychotics increased from 4% to 92% of all antipsychotics. In 1991, on average 2.9% of enrolees in a state were in capitated plans and only one state had mental health carveouts. By 2005, this number increased to 30% (for Medicaid), with 64% enrolees in any type of care. In that year, 33% of states had mental health care-outs.

Initially, capitated managed care was associated with a large increase in the share of psychotropic medications, although this result was not significant for SSRIs. A 10 percentage point increase in the use of managed care was associated with a 2.7 percentage point increase in the use of SNRIs and a 10.1 pp increase in the use of SGAs. Moreover, higher levels of utilisation of the new generation antipsychotics could be observed in the states with greater use of capitated plans, compared to states with no capitated payments. Including non-capitated care in the model weakens the relationship between managed care and new drug diffusion, while behavioural health carve-outs were associated with much smaller increases in the use of newer antipsychotics.

There are limitation to this study. First, because the data are aggregate, the models cannot be estimated at the sub-population level. Second, the DDD measure of drug use assumes constant doses of medications. Moreover, the data could not compare the intensive and the extensive margin. Finally, the study did not allow examination of off-label use of antidepressants. The study concluded that the strong growth in sales of the new generation psychotropic drugs was associated with the spread of capitated managed care.

Conclusions

Many researchers in economics and business schools may not be aware how widespread the use of antidepressants has become in modern society. The consumption of such pills has been approximately doubling every ten years and seems likely to double again over the next decade. It can be seen from the above that economics and management science has so far had little to contribute to an understanding of the modern phenomenon of the antidepressant pill. The published writings tends to be descriptive and straightforwardly empirical (as is natural, and valuable, in the early days of any scientific avenue).

We have attempted to review some of the recent social-science literature. Because antidepressants are, in a sense, a new way of purchasing less unhappiness, they are not a purely conventional kind of medicine. Nor are they a standard kind of product of the sort routinely sold in supermarkets and stores.

An ‘economics of antidepressants’ awaits to be developed. We suspect that antidepressants may eventually have to be modelled as a new form of consumption that lies in the currently grey area between medicines and consumer goods. The reasons are intrinsic to the nature of this modern commodity. First, in human beings, and probably in other kinds

of animals, the line between unhappiness and poor mental health is not an exact one. Where the definition of a medicine begins and ends, therefore, is blurry. In extreme cases of mental ill-health the case for antidepressants is an obvious one; there is evidence that such medication can produce real benefit to people who are profoundly ill. However, when antidepressants are able to be bought directly by regular citizens, in the way that aspirin and wine can be purchased, are antidepressants to be thought of as medicines or as items of lifestyle choice (as aspirin and wine typically are)? There is no clear answer to this question. Second, as we become better and better at removing the physical difficulties of human beings, it is to be expected that greater emphasis will emerge on removing the mental difficulties. The future of happiness and unhappiness pills is a complicated ethical one on which society, and social-science researchers, may soon have to focus more attention.

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