The EU Referendum and Mental Health in the Short-Term: A Natural Experiment using Antidepressant Prescriptions in England

Sotiris Vandoros[a,b]*, Mauricio Avendano[a,b] and Ichiro Kawachi[b]

[a] King's College London, London, United Kingdom
[b] Harvard T.H. Chan School of Public Health, Harvard University, Boston MA, USA

*Correspondence to: vandoros@hsph.harvard.edu King's College London, 30 Aldwych, London WC2B 4BG, United Kingdom

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Abstract

Background: Previous research has highlighted the impact of economic conditions and uncertainty on health and mental conditions. The unexpected result of the Brexit referendum in 2016 triggered high levels of economic uncertainty. We examined whether prescriptions for antidepressants increased after the referendum result, benchmarking them against other drug classes.

Methods: We used GP practice prescribing data to compile the total number of defined daily doses per capita every month in each of the 326 voting areas in England over the period 2011-2016. We used a difference-in-differences approach to identify the effects of Brexit on antidepressant prescriptions, compared to trends in a control group (antigout and iron preparations) that were unlikely to be associated with uncertainty and depression.

Results: Antidepressant prescribing continued to increase after the referendum but at a slower pace. Therapeutic classes used as controls demonstrated a decrease. The difference-in-differences approach shows that there was a relative increase by 13.4% in antidepressants compared to other therapeutic classes (DID coeff: 0.134; 95%CI 0.093–0.174).

Conclusion: Our results are open to different interpretations and should be treated with caution. This relative increase in antidepressant prescribing following the referendum may be attributed to increased uncertainty for certain parts of the population, but does not rule out an improvement in mood for others. Alternatively, some other factor, for example distraction, might have contributed to a decrease in the control therapeutic classes. A possible policy implication is that programmes for the promotion of mental health may need to intensify during periods of uncertainty.

Keywords: Brexit; Antidepressants; Mental Health; Differences-in-differences; England

1. Introduction

On 23 June 2016, the United Kingdom voted to leave the European Union, following an unexpected referendum result that caught the world by surprise. There was much at stake in the run-up to referendum: Leaving the EU was expected to heavily affect the British economy and society, including issues like free trade, immigration, social services, and rule of EU law. During the referendum campaign, it was claimed that Brexit would affect EU nationals' right to live and work in the UK, and the impact could affect UK and other nationals working for foreign companies that might decide to move to another EU country. The Brexit vote also sparked concerns about a possible economic downturn due to leaving the EU. Such uncertainty was captured by the Economic Policy Uncertainty Index, which reached unprecedented levels following the referendum [1]. For the majority, who voted in favour of leaving the EU, the result may have been a positive one. However, after the result, the Governor of the Bank of England warned of lower living standards, higher inflation, job cuts and even a recession as a result of leaving the EU [2-5] and argued that uncertainty has been building up over Brexit [6]. The "anxiety, unknowability of the changing political situation" after Brexit were even described in two recent songs by Mick Jagger, according to the artist [7].

While most changes are yet to materialise, an important question is whether the economic uncertainty and political upheaval following the Brexit vote led to psychological distress, similar to that registered following (positive or negative) shocks in other countries. For example, evidence suggests that terrorist attacks can affect mental health at the national level, and this effect is not limited to those who experience the attack [8].

Some might expect negative financial consequences due to leaving the EU [2-5], which may translate into negative mental health outcomes even before changes in employment materialise. For example, while an extensive literature shows that economic conditions are often associated with worse health [9-12] or suicide [13-18], a spike in suicides cannot always

be fully explained by increased unemployment. This increase in suicide rates may reflect uncertainty associated with poor macroeconomic performance, which may resemble to some extent the uncertainty associated with the Brexit vote. Likewise, the Brexit vote may also have forced households to rethink their future plans, particularly for older workers approaching retirement. For example, during the Great Recession of 2008, both in the US and Europe, job loss was associated with increased depressive symptoms among older workers [11], partly reflecting the uncertainty around retirement plans, the fear of negative effects of withdrawing from social networks, loss of a social role, and social stigma and psychological distress [19-26]. Likewise, the literature suggests that chronic job insecurity leads to poorer self-rated health reports and minor psychiatric morbidity (which appear to be long-term and remain even after uncertainty has decreased) [27] and an increase in healthcare utilisation [28]. If the Brexit vote increased the perception of job insecurity, we would expect some of these symptoms to emerge as a result. Overall, this literature suggests that job uncertainty and anticipation of future negative developments can impact mental health [29-32].

An extensive literature suggests that several measures of mental health seem to consistently worsen during economic recessions and improve during economic expansions. Most importantly, studies have consistently found that suicide increases during economic downturns and declines when the economy improves [13-18]. This association, however, may also vary across different regions and countries, with not all studies reporting countercyclical suicide mortality [33-35]. Worsening of other mental health outcomes such as depression has also been reported [35-37].

The Brexit vote offers a unique natural experiment to examine how a major societal event may influence the mental health of the population. What makes this case unique is that the 'treatment' was sudden and unexpected. As voting was coming to an end, even one of the leading proponents of the 'Leave' campaign had already conceded defeat [38]. While changes

in macroeconomic conditions or political party domination often change gradually and might be anticipated, in the case of Brexit, people woke up to an unexpected new uncertain situation on the morning following the referendum. This sudden nature of the intervention allows us to identify a start date of an intervention in our analysis, as opposed to cases where something builds up over time, thus helping make the empirical analysis clearer.

Understanding the potential psychological wellbeing consequences of the Brexit vote is important for two reasons. First, policy makers may underestimate the potential 'costs' of Brexit by focusing only on impacts on the economy or immigration, ignoring potential changes in psychological wellbeing that may in themselves influence economic performance and social cohesion. For example, the literature suggests that economic recessions lead to major changes in consumption behaviour that are largely explained by the psychological impact of the recession, which may in itself have an impact on the economy. Second, from a theoretical perspective, evidence of the psychological impact of Brexit may reveal some of the potential mechanisms that link economic uncertainty to mental health in general [15,31], as any possible effects of the referendum might be a specific example of a general phenomenon.

The objective of this study was to examine the impact of uncertainty following the Brexit vote on the use of antidepressant medication in England. We used detailed monthly data on prescription medication for antidepressant drugs for all 326 voting areas in England, and benchmarked prescriptions of antidepressants against prescriptions for other drug classes. We hypothesised that an event of this magnitude could led to an increase in psychological distress, which would translate in an increase in antidepressant medication.

2. Data and Methods

2.1 Data

The GP prescribing database, published by NHS Digital [39] provides data on the monthly number of presentations (boxes) of each drug prescribed by every practice in England. Prescriptions only enter the dataset after they have been dispensed. According to NHS Digital, all registered practices in England are included in the data. When a prescription cannot be linked to a practice, this is excluded, and such prescriptions account for 0.2% of the total sample [39]. We used monthly data for the period January 2011 - December 2016. As doses vary across drugs, simply aggregating the total number of milligrams could affect the results. To make data across different drugs comparable, the number of boxes was converted into the total number of defined daily doses (DDD) (as defined and provided by the World Health Organisation [40]), as follows: From the raw data included in the GP prescribing database, we first calculated the number of milligrams (number of pills in a box multiplied by the strength of each pill). Different calculations apply for different presentations of the same drug as they included different number of pills or different strengths. Subsequently, we divided the total number of milligrams by the defined daily dose (DDD), to obtain the number of DDDs of each drug prescribed by each practice in a month. These were then aggregated across each drug class, and summed by voting area in order to get the total number of DDDs per month prescribed in each voting area in England. There are 326 voting areas in England, with an average of 36.6 practices in each. The number of practices per area ranged between 3 and 355, and the average population per area was 169,534 people. A map of England with the locations of practices is presented in Figure A1 in the Online Appendix. The number of DDDs prescribed were divided by each voting area's population (provided by Public Health England) to estimate per-capita prescribing levels. The data were then combined with EU referendum results in each of the 326 voting areas in England (% leave and % remain), as provided by the Electoral Commission [41].

Antidepressants were defined based on ATC code N06A. For comparison (i.e. our control groups of prescriptions), we initially considered prescriptions for a number of

therapeutic classes: Iron preparations (ATC code: B03A) for treatment of iron deficiency anaemia, antigout preparations (M04A) for the treatment of gout, a type of inflammatory arthritis, insulins and analogues (A10A), blood glucose lowering drugs excluding insulins (A10B), plain lipid modifying agents (C10A), thyroid drugs (H03A) and muscle relaxants (M03C). ATC codes were obtained from the ATC/DDD system designed by the WHO Collaborating Centre for Drugs Statistics Methodology [42], a system that aims to serve as tool for monitoring drug utilisations. Summary statistics are presented in Table 1.

Antidepressant prescriptions were selected as an indicator of psychological distress. The other drugs were chosen because they reflect conditions that are not expected to fluctuate immediately depending on mental conditions. While all are useful comparison groups, and their pre- and post-referendum descriptive trends provide interesting patterns, only antigout and iron preparations met the formal common trend assumption, so only these entered the econometric model (see sections 3.1 and 3.4).

[Insert Table 1 here]

2.2 Methods

We used a difference-in-differences (DID) econometric approach, a quasi-experimental technique that compares outcomes in the 'treatment group' before and after exposure with pre- and post-treatment outcomes in a predefined control group. This is preferred to an approach that would examine trends in the treatment group only. By using a control group, we are able to control for secular trends in prescription medication that may not be the direct result of the Brexit vote. Our estimates thus examine whether the prescribing volume of antidepressants changed in the treatment period relative to the control group. There are three main (explanatory) dummy variables in a differences-in-differences model. One dummy represents

the treatment group, i.e. takes the value of 1 for the group that is exposed to the treatment (or intervention), and zero otherwise. A second dummy represents the treatment period, i.e. takes the value of 1 in the post-treatment period, and zero otherwise. The main variable of interest is the interaction of the two. A positive and statistically significant coefficient of the interaction term would suggest that the intervention has led to a change in relative trends between the two groups. The treatment and control groups do not need to demonstrate the same levels before the intervention, but they should have common trends.

Using linear regression, we employed a model at the voting area level using robust standard errors. The dependent variable is the natural logarithm of the number of DDDs per capita of a drug class prescribed in area i in period t. We included a dummy variable for antidepressant drugs, which constitutes the treatment group, taking the value of 1 for antidepressants, and 0 for the control group (antigout and iron preparations). A dummy for months from the referendum onwards (July 2016 onwards) was included to indicate the treatment period. The interaction term between these two dummies is the DID term, which shows what happens in the treatment group (antidepressants) after the treatment (the EU referendum) compared to the control group (other drug classes). We also included monthly time dummies (a dummy for each month in each year) as well as year dummies and region dummies (there are 9 broader Regions in England). We controlled for the average age of each voting area (because depression and voting may change by age), in quadratic form, because of the non-linear age effects.

In terms of months included in the sample, we followed two approaches: The first one limits the sample to only July each year, in order to compare the first month post-Brexit to the same calendar month in previous years. This would help isolate the effect on the first month following the referendum. The second approach takes advantage of all months in a year. We also examined heterogeneous effects across areas of England that were predominantly pro-Brexit (>60% pro-leave) and areas that were predominantly pro-remain (>60% pro-leave).

In sensitivity analyses, we controlled for voting area dummies (there are 326 voting areas in England) instead of regions, and quarterly time dummies, and we also performed a stepwise inclusion/exclusion of controls. In addition, instead of aggregating at the district level, we also performed the analysis at the individual practice level. The latter approach had some limitations, as we could not calculate dosages per capita, or control for age, as practices opened and closed during the study period.

Graphically, the common trend between antidepressants (treatment group) and antigout and iron preparations (control groups) is obvious in Figures 1 and 2 and confirmed empirically (see Section 3.4). The other classes were kept in the descriptive approach for information only.

[Insert Figure 1 here]

[Insert Figure 2 here]

3. Results

3.1 Trends

Figure 2 presents the number of DDDs prescribed per capita in voting areas in July every year per drug class. Of the classes presented in the graph, only antigout and iron preparations met the common trend assumption, so only these were included in the econometric approach (see section 3.4). However, apart from antidepressants (the treatment group) and antigout and iron preparations (the control group), we also indicatively included the other therapeutic classes described in Section 2.1. Prior to the referendum, antidepressants, antigout, iron, lipid, glucose and insulins all demonstrated an increase in July every year compared to

previous years. Antidepressant DDDs prescribed per capita increased after the referendum, although at a slower pace. At the same time, antigout, iron, lipid, glucose and insulins demonstrated a decrease right after the referendum, following a period of growth. It is interesting to see that per capita antidepressant prescribing continued to rise after the referendum, while other drug classes started decreasing after a number of years of continuous growth. Muscle relaxants were generally decreasing over most of the study period, a decrease that continued after the referendum. Antidepressant monthly trends are presented in Figure A2 in the Online Appendix.

3.2 *A differences-in-differences econometric approach*

Results of the difference-in-differences approach using robust standard errors are presented in Table 2. Column 1 presents the results when examining July each year only. The DID interaction term is positive and significant ($p<0.01$), suggesting that following the referendum, the volume of antidepressants prescribed increased by 13.4% relative to trends in other drug classes (DID coeff: 0.134; 95%CI 0.093 – 0.174).

[Insert Table 2 here]

Results were almost identical when including all months of the year in the analysis (column 2). The coefficient of the DID term is again positive and statistically significant, indicating that compared to the control group, relative antidepressant prescribing increased by 12.4%. ($p<0.01$; DID coeff: 0.124; 95%CI 0.108 - 0.139).

We also introduced an approach that compared areas that voted predominantly in favour of leaving (>60%) to those who voted predominantly in favour of remaining (>60%) (Table A1 in the Online Appendix). The interaction of the DID term is statistically insignificant,

indicating that the two types of areas demonstrated comparable relative increases in antidepressant prescribing.

3.3 Sensitivity Analyses

Results were robust to sensitivity analyses, including and excluding control variables, and introducing voting area dummies (Table A2, Online Appendix). Results are also confirmed by the model using observations at the practice level, rather than aggregating at the voting area level (Table A3, Online Appendix).

3.4 The Common Trend Assumption

Figure 1 suggests that there is a common trend prior to the referendum between the control group and the treatment group, at least when considering July every year. However, we also performed a formal test of the common trend assumption using intervention leads, similar to the approach followed by Autor 2003 [43] (Table A4 in the Online Appendix). Column 1 shows the results when considering July only, and all leads are statistically insignificant, suggesting that the common trend holds empirically. However, when considering all months (Column 2), the parallel trends assumption appears to be violated, so we should rely on the model with July only, rather than the one including all months.

4. Discussion

This paper studied the effect of the Brexit referendum result on prescribing patters of antidepressants, and benchmarked these against changes in prescriptions of other drugs unlikely to be associated with uncertainty and depression. When considering the number of antidepressant dosages prescribed, it appears that there was an increase after the referendum, but at a slower pace than previously. One could therefore initially suggest that the referendum led to a slowdown in the increase of antidepressant prescribing. However, using a differences-

in-differences approach, we found an increase in antidepressant prescriptions compared to other drug classes.

Our findings are open to different interpretations. The relative increase may reflect an increase in psychological distress, triggered by uncertainty relating to the results of the Brexit referendum. Alternatively, one could focus on the decrease in the control groups. This could perhaps be attributed to patient distraction in the aftermath of the referendum, regardless of whether they perceived it as a positive or negative development. Patients may have thus neglected to visit their GP or pharmacy, as distraction has been documented as a non-adherence factor [44-45]. Another interpretation could relate to physician behaviour, and although we are not aware of any shift in patients from specialists to GPs, we cannot rule out a substitution effect.

Overall, while our findings point towards a relative increase in antidepressant prescribing in terms of DDDs per capita, results should be interpreted with caution and further research is needed to examine whether there is any short-term relationship between the referendum result and mental health.

The findings do not seem to differ between pro-remain and pro-leave areas. In 'remain' areas, EU nationals were uncertain about their future in the country; people working for multinational or EU firms may be afraid of losing their job or relocating; while others may have been concerned about the prospects of the UK economy outside the EU. By contrast, in areas predominantly supportive of leaving the EU, most people might have felt satisfied with getting what they wanted, and perhaps received a boost in national pride, as the Leave win was even branded as marking 'independence day' [46]. Consistently, it has been shown that a boost in national pride can lead to higher levels of happiness [47]; and success in sports, that trigger national pride, can also lead to higher levels of subjective wellbeing [48]. However, in these 'leave' strongholds, in addition to uncertainty, some foreigners might have felt under pressure following the referendum result [49].

It is important to note that while our results indicate an average increase in antidepressants, antidepressant use relates to just part of the population. The increase in antidepressant prescribing does *not* mean that there is on average a worsening in mood in England. Our study does not capture the impact on mental health, mood or happiness for those who do not take antidepressants. The majority voted in favour of leaving the EU, and we should not ignore the possibility that for pro-Brexit voters, the post-referendum period might have been a positive one. Recent descriptive statistics released by the Office for National Statistics indicate an absolute increase in happiness in England in the months after the referendum [50]. These figures were not benchmarked against a control group, but even if happiness indeed increased on average in the population, this does not necessarily contradict our findings that particular population groups may have experienced higher levels of depression due to uncertainty.

This study is subject to limitations. First, the control group is not something that originates from a geographic area that was not subject to the treatment. While we would expect the drug classes that served as control group to generally be unaffected by uncertainty in the short run, these were still prescribed in England before or after the referendum, and we cannot rule out any potential contamination. Furthermore, the post-treatment period is short, as we wish to examine the short-term effects of the referendum result. Nevertheless, this might make the results vulnerable to noisy estimates. It is worth mentioning that we only capture what was prescribed by GPs, which means that we cannot observe any fluctuations in prescribing by specialists or in hospitals. In addition, we could not control for some individual characteristics, such as ethnicity etc. It is also important to note that we used DDDs to measure prescribing. Alternative approaches, such as number of prescriptions or number of boxes etc may not necessarily lead to the same results. In this case we chose to follow the DDD approach because it would capture not only any possible change in the number of patients taking medicines, but also any change in dosage. It would have also been worth studying relative trends in prescribing

of anxiolytics compared to control groups. However, prescribing of this class has been decreasing over the past few years, so trends prior to the referendum were completely different than those in the control groups. It is possible that antidepressants could, in some cases and to some extent, account for decreased anxiolytic use. Alternatively, the increase in antidepressant prescribing may be a response to symptoms relating to mood following the referendum, as more serious symptoms may be treated with antidepressants instead of other medications.

The existing literature covers the link between uncertainty and health [28-30], but previous studies often focus on long-term effects that are difficult to attribute to certain changes that occurred over time. Our study focused on an event that was unexpected, leading to an immediate shock. From a more general perspective, this paper shows that shocks at the national level can affect health and that uncertainty and expectations of future effects can have an impact on health in the short term.

The findings of this study have several important implications for policy. First, policies supporting mental health should intensify in periods of uncertainty. Second, our results suggest that the Brexit vote may have had consequences beyond changes in trade, immigration or the economy, influencing psychological wellbeing and leading to increased distress in the population. Most discussion on the Brexit vote focuses on political or economic issues, yet there has been limited discussion of the impact on individual health and wellbeing; our results contribute to addressing this gap. Finally, our study suggests that major political and economic shocks may have unanticipated consequences on population health, even before they directly affect employment, business or migration patterns [31]. This suggests that the anticipation of change may in itself be a risk factor for the use of antidepressants. Additional research is required to further investigate whether there are any direct or indirect effects on health and health-related behaviour and disentangle any potential impact of distraction and uncertainty.

> **What is already known on this topic**
>
> Events at the national level, such as elections and financial crises, can affect individuals' mental health.
>
> **What this study adds**
>
> Relative antidepressant prescribing increased in England after the Brexit referendum in June 2016, compared to other drug classes.
>
> This could be attributed to increased uncertainty for some parts of the population, but it does not rule out a possible improvement in mood for others.
>
> There are alternative possible explanations, and we cannot be sure that this relative increase in antidepressants is due to the referendum result.
>
> Programmes for the promotion of mental health may need to be intensified during periods of economic uncertainty or political upheaval.

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Ethics: This study does not involve human subjects, so ethics approval was not required.

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Tables

Table 1. Summary Statistics

Variable	Mean	Std. Dev.	Min	Max
antidepressant DDDs per capita per voting area	2.147	0.591	0.554	5.034
antigout preparation DDDs per capita per voting area	0.158	0.042	0.031	0.308
iron preparation DDDs per capita per voting area	0.768	0.269	0.105	2.242
antigout and iron preparation DDDs per capita per voting area	0.926	0.276	0.253	2.395
Antidepressant dummy variable	0.500	0.500	0	1
Brexit referendum onwards dummy variable	0.083	0.276	0	1
Differences-in-differences interaction term	0.042	0.200	0	1
population per voting area	166073	113806	2224	1128077
age per voting area	40.549	3.075	30.984	49.177

Table 2. Difference-in-differences regression results. Antidepressants (treatment class) and antigout and iron preparations (control classes)

	(1) July only	(2) Whole year
Dependent variable: Natural logarithm of total number of DDDs per capita, per voting area, monthly, 2011-2016		
antidepressants dummy variable (1 for antidepressants, which are the treatment group; 0 for other drugs that are the control group)	0.801***	0.833***
	[0.785 - 0.818]	[0.828 - 0.837]
referendum onwards time dummy. (1 from July 2016 onwards; 0 otherwise).	0.181***	-0.004
	[0.147 - 0.215]	[-0.031 - 0.024]
D-I-D interaction (antidepressants*referendum onwards)	**0.134***	**0.124***
	[0.093 - 0.174]	[0.108 - 0.139]
Average age per voting area	-0.164***	-0.167***
	[-0.232 - -0.096]	[-0.186 - -0.147]
Average age per voting area squared	0.002***	0.002***
	[0.001 - 0.003]	[0.002 - 0.002]
month dummies	-	yes
year dummies	yes	yes
region dummies	yes	yes
Constant	3.207***	3.155***
	[1.803 - 4.611]	[2.752 - 3.558]
Observations	3,912	46,944
R-squared	0.774	0.779
F-statistic	848.5	2169

The unit of analysis is the natural logarithm of the number of DDDs prescribed per capita in each voting area in England.
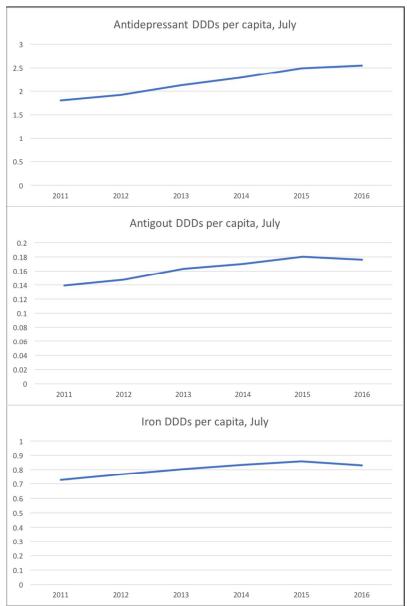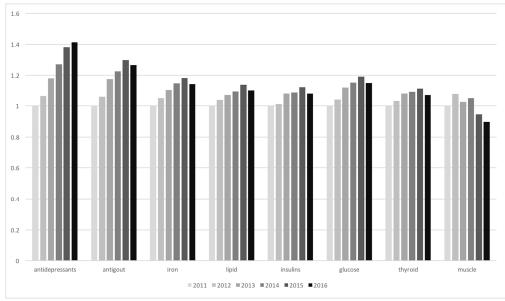Robust CI (95%) in brackets. *** $p<0.01$, ** $p<0.05$.

[FIGURE 1]

Figure 1 –Trends before and after the Referendum. Average number of DDDs per capita, month of July, years 2011-2015, all voting areas in England, based on data from NHS Digital (2018).

[FIGURE 2]
Figure 2. Average number of DDDs per capita, month of July, years 2011-2015, all voting areas in England, based on data from NHS Digital (2018).