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ARTICLE

The prevalence and consequences of support for off-label Ozempic prescriptions

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Abstract

Ozempic and related semaglutide drugs represent a popular new strategy to address obesity in the United States, yet uptake of these medications has sparked opposition highlighting concerns about off-label drug use policies, drug safety, supply shortages and cost. Public attitudes towards off-label prescribing by physicians broadly, and towards Ozempic in particular, in light of this opposition are unclear. To better understand public sentiment on this topic, we analysed data from a representative survey of 3,420 US adults conducted from 13 to 22 June 2023. Public attitudes towards off-label prescribing were split, with 46.3 percent supporting physician discretion to prescribe off-label. Importantly though, 58 percent of respondents were at least somewhat concerned about Ozempic supply shortages caused by off-label use and 63 percent were concerned about Ozempic safety in the context of off-label use. Further analysis from an embedded survey experiment shows that rhetoric highlighting safety (but not supply) concerns surrounding off-label Ozempic prescribing is associated with a significant drop in support for off-label use. These results suggest that the introduction of obesity drugs like Ozempic present a pharmaceutical industry-led path for combatting obesity, but rhetoric opposing these drugs could blunt public support and uptake.

Keywords: obesity; off-label prescribing; Ozempic; GLP-1

Obesity is a pressing medical and public health challenge. Obesity rates have doubled in over 70 countries since 1980 and almost a third of the global population is overweight or obese (GBD 2015 Obesity Collaborators, 2017; Chooi *et al.*, 2019). Alongside growing obesity rates, concerns have grown about the troubling proportion of individuals at risk for associated conditions including cardiovascular disease, diabetes, hypertension, certain cancers and poorer mental health (Anstey *et al.*, 2011; Czernichow *et al.*, 2011; Lauby-Secretan *et al.*, 2016; Powell-Wiley *et al.*, 2021). Obesity is particularly problematic in the United States, where the obesity rate increased from 30.5 percent in 1999–2000 to 41.9 percent 20 years later (CDC, 2022). Twenty-two US states have an adult obesity rate above 35 percent, and obesity is most prevalent among those with lower levels of education and less access to nutritious foods (CDC, 2023*a*). Obesity has considerable economic consequences as well. Estimates suggest that the medical costs of obesity in 2019 in the US were almost $173 billion, and those with obesity had an additional $1,861 in health costs compared to those at a healthy weight (CDC, 2022).

Considerable effort has therefore been put towards promoting health policy strategies to increase the proportion of individuals at a healthy weight. Many policy interventions have focused on improving the quality of individuals' diets. For example, efforts have emphasised

teaching children about healthy eating, encouraging healthier school lunches, taxing sugar sweetened beverages and providing caloric content on menus, among other policy interventions (Roberto *et al.*, 2015). Additional policy interventions have called attention to creating environments for learning healthy preferences, overcoming barriers to acting on healthy preferences, and encouraging individuals to reassess their food choices at the point of purchase (Hawkes *et al.*, 2015; Roberto *et al.*, 2015). As obesity rates continue to rise, however, alternatives to help individuals achieve a healthy weight are needed (Hawkes *et al.*, 2015; Roberto *et al.*, 2015).

One approach that has gained traction is the use of pharmaceutical interventions in the form of glucagon-like-peptide-1 (GLP-1) receptor agonists, a class of drugs used to treat type 2 diabetes and lower cardiovascular risk (Bald and Raber, 2023; Lovelace, 2023). Critically, growing evidence suggests that these medications can also be effective at reducing body weight. These medications stimulate insulin release which can lower glucose, change gastric emptying and nutrient absorption and suppress appetite (Choi and Vu, 2023; Lovelace, 2023). When taking these medications for weight loss, almost 80 percent of patients lose at least 5 percent of their body weight, with 42 percent losing at least 15 percent of their body weight (Bald and Raber, 2023). Recent evidence additionally suggests that GLP-1 drugs could help to reduce heart attacks and strokes (US Food and Drug Administration, 2024). Nearly 2 percent of Americans were prescribed semaglutide medications (GLP-1 drugs) in 2023, a 40-fold increase over the past 5 years (McPhillips, 2023). With long-term use of GLP-1 drugs by patients, weight loss is usually maintained, but once individuals stop taking these medications, weight gain is common.

Despite the benefits of these medications, concerns have started to mount related to drug shortages, drug safety and insurance coverage (Choi and Vu, 2023; Senior, 2023). GLP-1 drugs (and the drug Ozempic in particular) were designed to treat diabetes, but growing off-label use of the medications for weight loss – driven in part by celebrity endorsements and social media attention – have led to drug shortages in the US and the UK (Beba *et al.*, 2022; Tirrell, 2023; Han *et al.*, 2024). This has made it more difficult for those with diabetes to access needed medications and for those with obesity to begin taking these medications.

Another major concern ties to drug safety. GLP-1 agonists are associated with heightened risk of pancreatitis, bowel obstruction and gastroparesis (stomach paralysis) (Lovelace, 2023; Sodhi *et al.*, 2023). In addition, the European Union's European Medicines Agency (EMA) is actively investigating potential ties between the use of these medications and the risk of suicidal thoughts and self-injury (Constantino, 2023).

Finally, there have been efforts by insurance companies to limit the use of GLP-1 drugs for weight loss. With the GLP market estimated as producing costs as high as $90 billion a year by 2030, insurers are concerned about the high price tag of these medications in light of the prevalence of obesity and the possible need for long-term use of the medications (Gilbert, 2023). This has led many insurers to highlight the shortage and safety concerns noted above as justification for refusing to pay for GLP-1 drugs for weight loss, and threatening physicians with reporting to state licensure boards for off-label prescribing (Gilbert, 2023; Merelli, 2023). In the face of insurance denials, individuals are obliged to pay as much as $1,300 out-of-pocket or more per month for the medications in the US (Gilbert, 2023; Merelli, 2023).

Given the explosion of interest in GLP-1 receptor agonists as a path forward for weight loss and the related concerns tied to drug shortages, safety concerns and off-label (without FDA approval) use, more work is needed to understand public sentiment about the use of this class of medications for weight loss, and the conditions under which the public might be more (vs less) supportive of policies that enable off-label use (Murphy, 2023). This is an important area of research because public sentiment about the use of GLP-1 medications off-label could shape GLP-1 uptake by the public and the willingness of providers to prescribe the medication off-label. Equally important, public sentiment on these topics could shape lobbying and policy-making, including efforts to limit insurance company obstruction of GLP-1 prescriptions.

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Finally, this research has important implications for our understanding of public attitudes towards off-label prescribing and the pharmaceutical demand literature more broadly. Existing research suggests that between 20 and 40 percent of medications are prescribed off-label, even exceeding 50 percent for some medication types (Radley *et al.*, 2006; Blankart and Lichtenberg, 2022). Impacted by direct-to-consumer advertising increasing patient and provider awareness of prescription drugs and subsequent demand, this off-label prescribing can increase health care costs (Lakdawalla *et al.*, 2013; Dalton *et al.*, 2020; Blankart and Lichtenberg, 2022; Alpert *et al.*, 2023). Critically, despite the widespread prescription of medications off-label, very little is known about public sentiment towards off-label use. This research is designed to address that very question, providing valuable information which could help to guide policy-makers as they consider the extent to which the practice by providers should be regulated.

In stage 1 of the current study, we surveyed a representative sample of the US population and analysed the socio-political correlates of public support of physicians prescribing off-label Ozempic. In stage 2, we tested three conditions under which Americans are more vs less supportive of off-label prescribing policies via a randomised control trial embedded in this survey. The embedded trial assigned participants to receive different explanations used by the insurance industry questioning the use of Ozempic for weight loss; including: (a) information about Ozempic supply shortages, (b) information about safety concerns or (c) a control condition featuring no additional information.

1. Methods

We developed an online survey with an embedded randomised control trial, which we administered to a sample of 3,420 individuals in the United States. We administered the survey from 13 to 22 June 2023, via Lucid Theorem, a survey platform that uses quota sampling to produce demographically representative samples of the US population on the basis of racial/ethnic identity, gender identity and educational attainment (Coppock and McClellan, 2019). Data from Lucid are well suited for making associative claims (Jerit and Barabas, 2023), recover well-studied experimental effects (Peyton *et al.*, 2022) and scholars have relied on Lucid to study public sentiment and behaviour on a wide range of health policy topics (Kreps *et al.*, 2021; Motta *et al.*, 2023; Stauffer *et al.*, 2023).

In our survey, we assess Americans' attitudes about using Ozempic as a weight loss treatment, with a particular emphasis on understanding public concerns about the safety of off-label prescribing, and the scarcity that off-label prescribing by providers might engender. We chose Ozempic as the reference medication for our study of GLP-1 agonists due to the attention it has garnered in popular discourse and due to its status as a medication for which weight loss is a non-FDA-approved, off-label use.

2. Stage 1

2.1 Measures

We assess public support for off-label use via a question asking whether respondents believe that off label prescriptions should be (1) regulated by the federal government, (2) that doctors should have the discretion to prescribe drugs off-label as they see fit or (3) if they were unsure. In our descriptive analyses, this outcome measure was coded as a '1' if respondents believed that doctors should have the discretion to prescribe drugs off-label as they see fit, and as a '0' if they either believed that it should be regulated by the federal government or if they were unsure. We defined off-label use for participants as situations where doctors prescribe a drug to treat a condition not originally targeted by the drug manufacturer or if the manufacturer did not test the drug for that condition in the process of getting the drug approved for prescription. We then assessed concern about Ozempic safety and supply shortages based on survey questions with 4-point scales ranging

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from very concerned to not at all concerned. Our outcome measures for concern about Ozempic safety and supply shortages were both coded so that increasing scores reflected growing concern. The wording for each of these questions is available in Appendix A.

2.2 Analysis

We constructed multivariate models that assess the correlates of public support for doctors' abilities to prescribe prescriptions off-label, as well as potential Ozempic safety and supply concerns, via binary logistic (off-label prescribing) and ordered logistic (Ozempic safety and supply measures) regression. These models regress our outcome measures on dichotomous indicators of whether respondents have used Ozempic in the past as either a weight loss (off-label) or diabetes treatment, self-reported current health status (rated from poor to excellent) (see CDC, 2023*b*) and self-reported obesity status (based on a question asking whether a health care provider had ever told respondents they were obese). Models also include a series of demographic variables for sex, age, income, education, ethnicity, race, partisan identification and religiosity (see Appendix A). We limited our descriptive analyses to the proportion of participants assigned to the study's 'Control Condition' (see Trial description below), to avoid the possibility of experimental contamination effects, as we expected exposure to our 'Treatment Conditions' to influence concern about and/or support for off-label prescribing. These descriptive and correlational tests can be found in the section titled 'Observational Results'.

3. Stage 2

3.1 Randomised trial

We were interested in the *conditions under which* people might be more likely to support or oppose policies that permit off-label prescription. Correspondingly, we embedded a randomised controlled trial (RCT) in our survey aimed at identifying whether arguments commonly made in opposition to off-label Ozempic prescribing might impact public opinion. In the RCT, respondents were first asked to read a short passage introducing the concept of 'off-label' prescribing. Respondents were then randomly assigned to either (a) read additional information highlighting the possibility that off-label prescribing of Ozempic could lead to pharmaceutical supply shortages ('Shortage Condition'), (b) read additional information about safety concerns arising from off-label use ('Safety Condition'), or (c) read no additional information at all ('Control Condition'). Each condition employed in our experiment mirrors language used by the insurance industry questioning the use of Ozempic for weight loss and language used by those concerned about drug shortages of Ozempic caused by off-label use, as reported in each case by the media. Individuals were not given information tied to the source of these criticism (i.e. not told that these were insurance industry critiques) and were merely presented with the arguments used in opposition to Ozempic and its off-label use. An overview of our study's experimental design is summarised in Table 1.

After being asked to read one of our experimental conditions, participants answered a series of questions probing whether they believed that medical professionals should be able to prescribe Ozempic 'off-label' (see the final row in Table 1 for full question wording), which serves as the primary outcome variable in our RCT analysis. Respondents were also asked to rate their levels of concern about safety and supply shortage issues that might arise from off-label prescribing, which serve as manipulation checks in our experimental analyses; i.e. to determine if exposure to each experimental treatment raised the types of concerns that we would expect (safety concerns in the Safety Condition, supply concerns in the Shortage Condition). For consistency across tests in our experimental analysis, and due to computational limitations (i.e. that software packages like MEDIATE for Stata require hypothesised mediators to be measured at either the interval or dichotomous – and not ordinal/categorical – level) associated with the types of

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Table 1. Overview of Ozempic rhetoric randomised control trial

Explanatory text (shown to all)

As you may know, some doctors prescribe medicine for their patients for 'off-label' use. 'Off-label' use refers to situations where doctors prescribe a drug in order to treat a condition not originally targeted by the drug manufacturer or if the manufacturer did not test the drug for that condition in the process of getting the drug approved for prescription.

Control

We'd like to know more about your thoughts on off-label prescribing. Some people think that doctors should have the discretion to determine when they prescribe drugs for off-label purposes. Others think that doctors' abilities to prescribe off-label should be regulated by the federal government.

Shortage

As you may know, some doctors prescribe medicine for their patients for 'off-label' use. 'Off-label' use refers to situations where doctors prescribe a drug in order to treat a condition not originally targeted by the drug manufacturer or if the manufacturer did not test the drug for that condition in the process of getting the drug approved for prescription.

For example, although the drug Ozempic is designed to manage the blood sugar level for people living with diabetes, some doctors are prescribing the drug to stimulate weight loss in people who are overweight. While preliminary research suggests that Ozempic may be effective at helping overweight patients lose weight, Ozempic was not approved for this purpose. Doctors' off-label prescribing of Ozempic may be contributing to supply shortages of the drug, making it more difficult for people with diabetes to get Ozempic.

We'd like to know more about your thoughts on off-label prescribing. Some people think that doctors should have the discretion to determine when they prescribe drugs for off-label purposes. Others think that doctors abilities to prescribe off-label should be regulated by the federal government to prevent supply shortages.

Safety

As you may know, some doctors prescribe medicine for their patients for 'off-label' use. 'Off-label' use refers to situations where doctors prescribe a drug in order to treat a condition not originally targeted by the drug manufacturer or if the manufacturer did not test the drug for that condition in the process of getting the drug approved for prescription.

For example, although the drug Ozempic is designed to manage the blood sugar level for people living with diabetes, some doctors are prescribing the drug to stimulate weight loss in people who are overweight. While preliminary research suggests that Ozempic may be effective at helping overweight patients lose weight, Ozempic was not approved for this purpose. Doctors' off-label prescribing may pose a risk to patient safety by giving patients Ozempic outside its intended and approved use.

We'd like to know more about your thoughts on off-label prescribing. Some people think that doctors should have the discretion to determine when they prescribe drugs for off-label purposes. Others think that doctors abilities to prescribe off-label should be regulated by the federal government to prevent safety issues.

Outcome variable measurement (shown to all)

What about you? Do you think that:

1. *Doctors' abilities to prescribe drugs 'off-label' should be regulated by the federal government*
2. *Doctors should have the discretion to prescribe drugs 'off-label' whenever they see fit*
3. *I am not sure*

Manipulation check variable measurement (shown to all)

How concerned are you about supply shortages of the drug Ozempic that might result from off-label prescriptions?

1. Very concerned
2. Somewhat concerned
3. Not too concerned
4. Not at all concerned

How concerned are you about the safety of off-label use of the drug Ozempic?

1. Very concerned
2. Somewhat concerned
3. Not too concerned
4. Not at all concerned

mediation tests we employ, we dichotomised the safety and shortage concern measures in our experimental analyses – as well as the RCT's primary outcome variable – such that indicating any level of concern or support for off-label prescribing takes on a score of 1, and 0 otherwise.

We analysed our RCT via series of logistic regression models that regress respondents' concerns about off-label safety and supply issues on a series of dichotomous indicators of experimental treatment assignment (with the Control Condition serving as an analytic comparison), while controlling for whether respondents had ever used GLP-1 agonists for on- or off-label purposes. Controlling for prior use of the drug allows us to account for the possibility that off-label users are, as a result of their experiences, less likely to be concerned about safety considerations, and/or that on-label users are comparatively more worried about their ability to access the drug in the future due to shortages. These models serve as confirmatory *manipulation checks* of our study's experimental design. We then construct an analogous logistic regression model that is otherwise identical to the manipulation check analyses but swaps the safety and shortage concern variables described above with the study's primary outcome variable (support for off-label prescribing). This test serves as a test of the study's *experimental treatment effects*.

To further test whether the concerns raised by our experimental treatments are responsible for any treatment effects we might observe, we supplement the models listed above with formal mediation tests, using the MEDIATE commands in Stata 18. Given the dichotomised measurement of both the outcome and mediator variables, we estimate all steps of the mediation equation using logistic link functions. These tests allow us to decompose the direct effects of experimental condition assignment on off-label prescribing attitudes vs indirect effects attributable to raising concerns about off-label safety and supply issues. While some (see Green *et al.*, 2010) raise concerns about mediation analysis applied in observational settings (where the hypothesised mediator may be influenced by unobserved confounds), our approach overcomes this issue by directly manipulating the study's hypothesised mediators (safety and supply concerns) via experimental treatment exposure.

To limit the impact of potential inattentiveness of survey participants (Ternovski and Orr, 2022), we exclude respondents who finished our survey – which was designed to be approximately 10 min in length – in *less than half* of its median completion time. Doing so excludes $N = 232$ individuals from our analysis who completed the survey in less than 3 min (half of the survey's median completion time). We found no statistically significant differences in exclusions for inattentiveness across conditions.

4. Results

4.1 Observational results

We found that 46.3 percent of respondents in the Control condition agreed with the statement that doctors should have the discretion to prescribe drugs off-label whenever they see fit. We further found that 37.7 percent of respondents believed that doctors' abilities to prescribe drugs off-label should be regulated by the federal government and 16 percent of respondents were unsure. In our multivariate analysis in Model 1 of Table 2, we find that moving from low to high levels of income increases the probability of agreeing that doctors should have the discretion to prescribe drugs off-label from 39 to 56 percent, a 17-percentage point (pp) increase. Similarly, a one standard deviation increase in age increases the odds of agreeing that doctors should have the discretion to prescribe off-label by 7 pp (from 43 to 50 percent) and moving from identifying as a Strong Democrat to a Strong Republican resulted in a 17 pp increase (from 39 to 56 percent). Conversely, moving from poor health to excellent health decreased the likelihood of supporting off-label use by 17 pp and increasing religiosity reduced it by 10 pp.

In total, 19.7 percent of our control condition sample was very concerned about the possibility of supply shortages of Ozempic caused by off-label use, with over half (58 percent) at least

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Table 2. Correlates of attitudes towards the use of prescription drugs off-label

Variables	(Model 1) Docs prescribe off-label	(Model 2) Ozempic shortage concerns	(Model 3) Ozempic safety concerns
Female	1.15	1.23*	1.09
	(0.154)	(0.147)	(0.130)
Age	1.01**	0.99**	1.00
	(0.004)	(0.004)	(0.004)
Income	1.07**	1.05*	1.03
	(0.031)	(0.027)	(0.027)
College degree	0.91	1.23*	1.09
	(0.126)	(0.153)	(0.135)
White non-Hispanic	1.57*	1.30	0.85
	(0.426)	(0.308)	(0.200)
Black non-Hispanic	0.94	1.48	1.23
	(0.318)	(0.432)	(0.360)
Hispanic	1.16	1.45	0.89
	(0.354)	(0.385)	(0.235)
Republican	1.12***	0.91***	0.88***
	(0.034)	(0.025)	(0.024)
Religiosity	0.90**	1.28***	1.28***
	(0.045)	(0.057)	(0.057)
Overall health	0.84**	1.04	1.15**
	(0.060)	(0.066)	(0.074)
Obesity	1.03	0.93	0.79
	(0.174)	(0.140)	(0.120)
Oz for weight (ref: no use)	0.63	4.39***	1.79*
	(0.232)	(1.486)	(0.550)
Oz for diabetes (ref: no use)	0.77	5.07***	2.04**
	(0.276)	(1.743)	(0.678)
Constant	0.44*		
	(0.196)		
Observations	1032	1036	1033
Pseudo R^2	0.05	0.05	0.04

Standard errors in parentheses.
***$p < 0.01$, **$p < 0.05$, *$p < 0.10$.
Notes: All models present coefficients for odds ratios. Model 1 relies on binary logistic regression and Models 2–3 rely on ordinal logistic regression. Model 1's dependent variable is coded as 1 if individuals believe that doctors should be able to prescribe medication off-label. Model 2's dependent variable asks respondents how concerned they are about supply shortages of the drug Ozempic that might result from off-label prescriptions. Model 3's dependent variable asks respondents how concerned they are about the safety of off-label use of the drug Ozempic. All results are based on only the control condition of the randomised control trial embedded in our survey.

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Table 3. Manipulation check and experimental treatment effect summary

Test type	Outcome	Predictor	β	p	% Mediated (direct effect of condition assignment; indirect effect via short/safety concerns)
Manipulation check	Short. concerns	Short. condition	0.14	0.11	N/A
Manipulation check	Safety concerns	Safety condition	0.17	0.05	N/A
Experimental treatment effects	Off-label support	Short. condition	−0.11	0.18	N/A
Experimental treatment effects	Off-label support	Safety condition	−0.17	0.05	21% (0.05; 0.01)

Notes: Parameter estimates are derived from the logistic regression models described above (see: Analytical Strategy) and presented in full in the Supplementary Materials. Corresponding p values are two-tailed. Mediation analyses are provided only for those treatment effects attaining two-tailed statistical significance. Full model output can be found in the Supplementary Materials. All models exclude $N = 232$ respondents who completed the survey in under half of the study's median completion time.

somewhat concerned about supply shortages and only 10.6 percent not at all concerned about the issue. Model 2 of Table 2 suggests that concern was particularly high among those actively using Ozempic for either weight loss or diabetes, who were more likely – by a factor of 28 pp (from 18 to 46 percent) and 32 pp (from 18 to 50 percent), respectively – to be very concerned about supply shortages as compared to those not using Ozempic. Simultaneously, we found that a one standard deviation increase in age decreased concern by 4 pp and moving from being a strong Democrat to a strong Republican decreased supply shortage concerns by 8 pp (from 24 to 16 percent).

Additionally, we found that 23.3 percent of respondents in the control condition were very concerned about the safety of off-label use of Ozempic, with 62.6 percent at least somewhat concerned and only 6.5 percent of respondents not at all concerned about the safety of off-label use. In multivariate models, we found that individuals with diabetes using Ozempic were 14 pp more likely to be worried about off-label safety concerns than those not taking Ozempic (from 22 to 36 percent, respectively). Similar effects only approach significance ($p = 0.06$) among those who were using Ozempic for weight loss.

5. Experimental results

5.1 Manipulation check

In Table 3, we report that exposure to our safety treatment was significantly associated with increased concern about the safety of off-label prescribing ($= 0.17$, $p = 0.05$). We detect a similarly-signed ($\beta = 0.14$) pattern of effects for the shortage treatment on shortage concerns, although this effect falls just short of conventional two-tailed significance ($p = 0.11$). Table 3 presents our manipulation check and experimental treatment effect summary and Appendix B presents the full model output used to produce Table 3.

5.2 Experimental treatment effects and mediation analysis

Next, we assess whether exposure to our experimental treatment materials was associated with greater opposition to off-label prescribing. The results are summarised in the third and fourth rows of Table 3 and provided in full in the Supplementary Materials. We found that exposure

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Figure 1. The effects of safety condition assignment (vs control) on predicted support for off-label prescriptions.
Note: Predicted probabilities presented (bars) with 95 percent confidence intervals in parentheses. Predictions are derived from the models summarised in rows 3–4 of Table 1 (presented in full in the Supplementary Materials), and hold all other covariates at their sample means. All models exclude $N = 232$ respondents who completed the survey in under half of the study's median completion time.

to the study's safety treatment ($= 0.17$, $p = 0.05$), but not the shortage treatment ($\beta = -0.01$, $p = 0.91$) was associated with increased opposition to off-label prescribing.

As parameter estimates from maximum likelihood models can be difficult to interpret on their own, Figure 1 presents these results as more-tractable predicted probabilities. There, we find that – holding all other covariates at their sample means – exposure to the study's safety treatment (vs control) was associated with a 4-pp decrease in the probability of supporting off-label prescribing; from 46 percent (95 percent CI: 44, 49) in the control condition, to 42 percent (95 percent CI: 39, 45) in the safety condition.

In analyses presented in the Supplemental Materials, we find that 36 percent of the total effect (TE) of exposure to the study's safety condition (TE = −0.04; calculated by adding the treatment's direct effect (DE = −0.03) of off-label support plus the indirect effect (IE = −0.01) channelled through safety concerns) is attributable to increased concern about patient safety. Taken together, these results imply that our safety treatment which was modelled after concerns posed by the insurance industry and other discourse was effective at engendering concern about off-label prescribing, which were in turn associated with opposition to off-label prescribing.

6. Discussion

New approaches for helping Americans achieve healthy weights will play an important role in confronting the troubling rates of obesity in the United States, and its associated consequences for comorbidities, health outcomes and health care costs. While recent policy interventions tied to improving diets and creating environments that encourage healthy choices have had positive impacts, they have thus far been insufficient to stem the tide of weight gain. The introduction of GLP-1 agonists and related medications presents a pharmaceutical industry-led path for combatting obesity, but excitement over the results of promising early returns has been blunted by considerable opposition from insurance companies due to high costs, concerns over supply shortages and safety concerns tied to off-label drug use.

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Our research investigates public attitudes towards these issues, as well at how rhetoric currently being used by insurance companies might impact public sentiment. We find that 46.3 percent of Americans in our control condition believe that doctors should have the discretion to prescribe drugs off-label whenever they see fit, with 53.7 percent of Americans either believing that doctors abilities to prescribe off-label should be regulated by the federal government (37.7 percent) or unsure about off-label prescribing (16.0 percent).

With off-label prescribing accounting for 20–40 percent of prescription use in the United States and less than 50 percent of Americans in support of physician discretion (Radley *et al*., 2006; Blankart and Lichtenberg, 2022), our results suggest that regulation of off-label prescribing by policymakers could be warranted. Decades of public opinion research demonstrate that politicians are responsive to public opinion (Druckman and Jacobs, 2006; Shapiro, 2011) and these findings suggest only moderate support for the level of discretion physicians currently possess. Of course, it is vital to recognise that a single metric of public sentiment alone should not guide US policymaking, especially in a space with public uncertainty – with 16 percent of respondents unsure of their position. We believe these results serve as an important first step in this line of inquiry and that additional research in this space is needed to continue to better understand public preferences on off-label prescribing broadly.

With regard to GLP-1 drugs, we additionally found in descriptive analyses that concern over supply shortages and the safety of Ozempic resulting from off-label use was common. Importantly, however, our experiment demonstrates that rhetoric tied to Ozempic shortages and safety concerns had different effects on off-label prescription support. Highlighting safety concerns surrounding off-label Ozempic prescribing was associated with a drop in support for off-label use. We saw similarly signed results for messages highlighting supply shortage concerns but note that these results failed to reach conventional levels of statistical significance. Collectively, our experimental results suggest that actors opposed to the growth in GLP-1 drug use might be particularly likely to persuade Americans to oppose off-label use by integrating potential safety concerns into their messaging strategies. Highlighting that prescribing Ozempic outside of its intended and approved use could pose a risk for patient safety appears to call into question the trust that the public puts into the institutions and systems that ensure that drugs are safe, with negative consequences for off-label prescribing support. Equally important, our evidence suggests that those opposed to off-label GLP-1 use may experience less success highlighting shortage concerns and their potential impact on those with diabetes who need the medications.

Our results also point to the correlates of public support for off-label prescribing as well as concerns about Ozempic shortages and safety. We find that Republicans are more supportive of giving physicians discretion to prescribe drugs off-label and are less concerned about shortage and safety issues tied to Ozempic. These findings could result from conservative beliefs about opposition to government regulation and market interference (Chen and Goren, 2016). We find a similar pattern of results for our age measure, with older individuals more likely to support off-label prescribing and less likely to be concerned about supply shortages of Ozempic.

Interestingly, we observe the opposite pattern of results for more-religious individuals who are not supportive of physicians prescribing off-label and are significantly more likely than non-religious individuals to be concerned about Ozempic supply shortages and safety. A similar pattern holds based on individual health, with healthier respondents less supportive of off-label prescribing but more concerned about the safety of off-label Ozempic use. Finally, we find that wealthy individuals support off-label prescribing and that individuals who take Ozempic for either weight loss or diabetes are more concerned about both supply shortages and drug safety. Further investigating these correlates and their origins is an important direction for future research.

Finally, our results have important implications for the literature on pharmaceutical demand. While prior work has demonstrated that off-label drug use is common (Radley *et al*., 2006;

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Blankart and Lichtenberg, 2022), our research shows that the public is decidedly split on whether doctors should have the current discretion they do to prescribe off-label. Equally important, our work suggests that while policy shocks can serve to increase pharmaceutical demand (Lakdawalla *et al.*, 2013; Alpert *et al.*, 2023), negative rhetoric can have the opposite effect and heighten concerns about off-label prescribing. Exploring the impact of rhetoric on changes in prescribing patterns is a valuable direction for future research on pharmaceutical demand.

There are several limitations of this study. We recognise that as a cross-sectional study, we are unable to assess changes in attitudes towards off-label prescribing and GLP-1 agonists over time. Given the fast-paced evolution of celebrity endorsements, media attention, accumulating safety data and provider and insurer behaviour in this area, our study cannot determine how a wide range of social, political and economic forces might contribute to attitude change over time. Relatedly, this fast-paced evolution prevents us from exploring new GLP-1 concerns tied to out-of-pocket costs or the use of compounding pharmacies to access Ozempic and other drugs in short supply, which emerged after our analysis was performed (Gilbert, 2023). Future research which explores additional messaging strategies would be beneficial. We note that this future work should highlight not just concerns, but also provide insight into what types of messaging strategies might *promote* public acceptance of off-label prescribing broadly, or of GLP-1 drugs in particular.

In addition, our obesity measure is limited in that it relies on self-reported data rather than a clinical diagnosis. Self-reported measures may be inaccurate indicators of clinical diagnoses due to biased recall or social desirability pressures. Future research may therefore benefit from supplementing self-reported data with more-objective (yet imperfect) weight and obesity indicators, such as BMI. Our analysis is also limited in its reliance on a demographically representative quota sample. While we have already pointed to a large body of evidence suggesting that Lucid and other similar survey platforms are 'fit for purpose' for the types of correlational and experimental analyses we provide (Peyton *et al.*, 2022; Jerit and Barabas, 2023; Motta *et al.*, 2023; Murphy, 2023; Stauffer *et al.*, 2023), they are less well-suited to provide generalizable population estimates of just how many Americans support or oppose off-label prescribing (Jerit and Barabas, 2023). For this reason, we would encourage researchers to make an effort to replicate studies like this one in nationally representative survey data.

It is also important to note that while our manuscript captures public attitudes about whether doctors' abilities to prescribe drugs off-label should be regulated by the federal government, that phrasing is quite broad. Participants could bring different considerations to mind as they consider 'regulation' by the federal government in this space. As such, we encourage future research which explores public sentiment about different paths towards federal regulation in the future.

Despite these limitations, this research still has important implications for public health. Using a demographically representative sample, we have illustrated split public attitudes in the American public about the ability of physicians to prescribe drugs off-label, which could help to shape future discussions of discretion to physicians in this space. In the specific case of Ozempic, off-label prescribing raises concerns among Americans about drug safety and drug shortages. This is exacerbated by the rhetoric currently in use by the insurance industry calling into question drug safety. For Ozempic and other GLP-1 agonist drugs to serve as a viable widespread path forward on obesity, public health interventions to overcome safety and supply concerns must be prioritised.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S1744133124000306.

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