**Title**
Decline in Physicians' Response to a Non-Interruptive Clinical Decision Support Alert



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# Decline in Physicians' Response to a Non-Interruptive Clinical Decision Support Alert

A thesis submitted in partial satisfaction of the requirements for the degree Master of Science in Clinical Research

by

Douglas A. Murad

2021

ABSTRACT OF THE THESIS

Decline in Physicians' Response to a Non-Interruptive Clinical Decision Support Alert

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Master of Science in Clinical Research

University of California, Los Angeles, 2021

Professor Douglas Bell, Chair

**Introduction:** Clinical decision support (CDS) alerts have shown promise in improving health care quality and patient outcomes. Although repeated exposure to alerts may lead to declined responses by physicians, known as "alert fatigue," little is known about how the introduction of competing alerts may affect uptake over time.

**Methods:** We examined alert responses over time and identified factors associated with decreased alert effectiveness. We analyzed the audit data from all occurrences of a CDS alert at a single, large academic health system. For patients screening positive for depression during ambulatory visits, a non-interruptive CDS alert is presented to the physician, offering a number of appropriate documentation actions. Alert uptake was defined as the selection of any option offered within the alert during the patient encounter. We assessed the effect of (1) the number of competing clinical guidance alerts presented during the same encounter and (2) the total number of all clinical guidance alerts that the same provider had seen in the prior 90 days, on the probability of depression screen alert uptake, adjusting for physician and patient characteristics.

**Results**: A total of 55,649 office visits involving 418 physicians and 40,474 patients between September 1, 2017, and February 28, 2021, were included. After adjustment for potential confounders, physicians who had seen the most CDS alerts in the prior 90 days were less likely to utilize the depression alert than those who had seen it the least (adjusted uptake rate, 19.8% at the highest quartile versus 39.3% at the lowest quartile; adjusted odds ratio, 0.38; 95% CI 0.35 to 0.42; $p<0.001$). The negative impact of competing alerts in the same visit on depression alert uptake was only seen among physicians in the middle two quartiles of alert exposure in the prior 90 days.

**Conclusion:** Among physicians at a single large academic health care system, the declining use of a non-interruptive depression alert was strongly associated with the provider's 90-day prior exposure to alerts. Health systems should monitor providers' recent alert exposure as a measure of potential alert fatigue.

The thesis of Douglas A. Murad is approved.

Yusuke Tsugawa

David Elashoff

Douglas Bell, Committee Chair

University of California, Los Angeles

2021

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# LIST OF ACRONYMS

- EHR: Electronic health record
- CDS: Clinical decision support
- PHQ-9: Patient health questionnaire-9
- GLMM: Generalized linear mixed-effect model
- ICD: International classification of diseases, $10^{th}$ revision
- PCP: Primary care physician
- ANOVA: Analysis of variance
- aOR: Adjusted odds ratio

# SUPPLEMENTARY MATERIALS

# ACKNOWLEDGEMENTS

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# INTRODUCTION

Although research shows that receipt of healthcare services supported by guidelines can lead to improved outcomes, not all patients receive evidence-based care. Indeed, prior studies have shown that patients receive guideline-directed treatment only half of the time.[1, 2] It has been demonstrated that the provision of appropriate care may be deleteriously impacted by time pressure on physicians.[3, 4] As part of an institution-wide effort to improve the quality of care by mitigating these factors, our institution developed a clinical decision support (CDS) system that enables physicians to rapidly attest their evaluation of patients with positive depression screens. While CDS has been well-received by physicians, systems generally have been met with mixed success in terms of their impact on the quality of care, despite playing a central role in the Medicare and Medicaid Promoting Interoperability Program. In particular cases, they have been shown to improve patient safety,[5, 6] lower costs for health care systems,[7] improve adherence to clinical guidelines,[8, 9] increase the quality of clinical documentation,[10] and heighten diagnostic accuracy.[11] However, there remain persistent criticisms related to alert fatigue,[12] alert inappropriateness,[13] and workflow fragmentation resulting in increased cognitive load.[14]

These shortcomings have been blamed for high alert override rates,[15, 16] motivating considerable research to improve CDS usability.[17] However, even finely crafted alerts must operate within a milieu of competing alerts. While it has been shown that alert uptake may be inversely related to the firing frequency of the individual alert, [18] it is not clear how the likelihood of provider uptake of a single alert is altered by the overall volume of alerts recently seen by a provider.

In this context, the aim of this study is to describe (1) long-term, longitudinal uptake rates of a non-interruptive, positive depression screen CDS alert (2) and to assess the extent to which uptake is modified by the overall volume of clinical guidance alerts seen by the provider over the preceding 90 days (*recent alert count*) or (3) by the number of competing alerts seen during the same encounter (*competing alert count*).

# METHODS

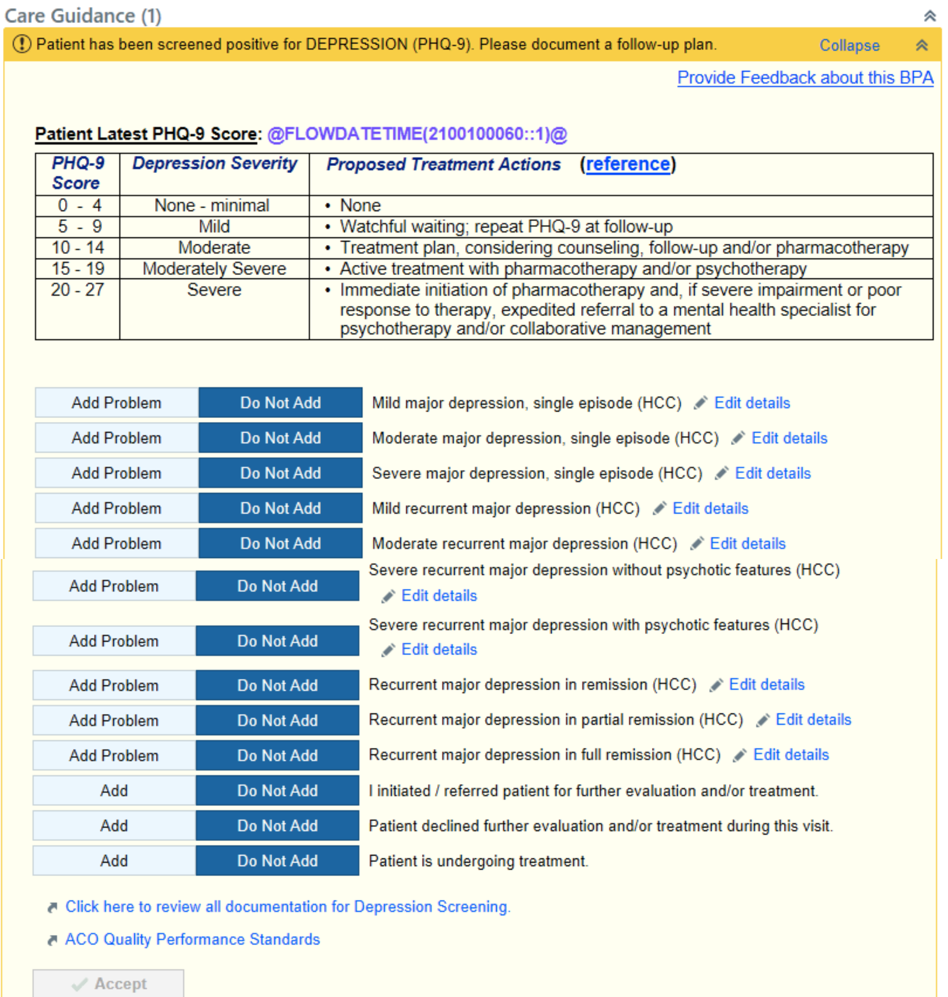
## Clinical Decision Support Tool

Screening with the PHQ-9 (Patient Health Questionnaire) depression severity measure [19] takes place during the rooming process of many ambulatory care clinics at UCLA Health. A score greater than 4, suggestive of at least mild depression, triggers a non-interruptive alert in the provider's EHR navigation window. Inside the alert, providers may choose to add one of ten depression diagnoses to the patient's problem list, click on a link for further clinical guidance, or attest to: initiation of depression treatment, referral for further evaluation, patient refusal of evaluation or treatment, or whether the patient is already undergoing treatment (Figure 1). The previous existence of depression on the patient's problem list did not suppress alert firing.

## Data

Every depression alert firing associated with an appointment between September 1, 2017 and February 28, 2021 was extracted from the relational auditing database supplied by the EHR vendor. Any actions taken upon any of the alert firings during the patient encounter were noted. Physician and patient characteristics were retrieved from separate tables of the same database. All problem lists, encounters, billing, or past medical history diagnoses made on or prior to the encounter date were collected from the patient's record. After removal of depression diagnoses

Figure 1: Screenshot of Depression Screening Clinical Guidance Alert*




Screenshot courtesy of © 2020 Epic Systems Corporation.
*The first ten pushbuttons allow the user to rapidly add a new depression problem to the patient's electronic health record. The last three push buttons allow the user to quickly attest that the depression screen has been reviewed and documents follow-up for quality reporting.

made on the office visit date, the remaining codes were used to automatically generate [20] AHRQ-weighted Elixhauser comorbidity scores [21] for each patient encounter. Encounters with any alert firings shown to residents, nurse practitioners, scribes, or other ancillary staff were excluded. Depression alerts that did not fire on the day of the encounter were not included. Encounters with patients less than eighteen years of age were excluded.  For consistency over time, only alerts shown during office visits were included. Physicians with less than ten encounters with positively screened patients over the entire study period were excluded.

## Alert uptake

The primary, binary outcome of physician alert uptake was calculated at the level of each unique patient office visit. The decision to add a new depression problem, to click on an informational link, or to select an attestation button within the alert was denoted as positive alert uptake.

## ‘Recent Alert Exposure’ and ‘Competing Alert Count’

Recent alert exposure was defined as the number of clinical guidance alerts of any kind seen by the physician in the 90 days prior to each encounter. The competing alert count was defined as the count of all other clinical guidance alerts presented to the physician during the encounter in which a depression alert was seen. Any use of the term ‘alert’ in this paper refers to clinical decision support tools of the clinical guidance variety. Medication alerts were not measured.

## Descriptive analysis of alert uptake rates over time

In order to visualize unadjusted, longitudinal alert performance data, the percent of depression alert encounters with any uptake was plotted on a monthly basis. In parallel, the average number of competing alerts shown to the provider during each encounter with a depression alert was plotted. Finally, the average number of alerts shown to the provider over the preceding 90 days was graphed over the same time interval.

## Statistical analysis

First, we used generalized linear mixed-effect models (GLMM) with logit link (physicians and patients as random intercepts) at the level of each individual encounter associated with a depression alert. Alert uptake was used as the binary outcome variable with recent alert count and competing alert count as covariates, and physician and patient characteristics as adjustment variables. [22] We then calculated adjusted alert compliance rates using the marginal standardization method by holding covariate values at their means and varying the covariates of interest.[23]

We also investigated the relationship between recent alert exposure and competing alert count on alert uptake during each visit. An interaction term between the two variables was added to the original model. ANOVA testing between the main model with and without the interaction term was performed. The marginal effect on alert uptake probability was plotted for the two interacting variables in the model.

## Adjustment variables

Physician characteristics used as adjustment variables included sex, the decade of medical school graduation, primary specialty, and primary care relationship with the patient. Patient characteristics included sex, age, antidepressant prescription in the last year, active depression diagnosis on the problem list, and PHQ-9 score triggering the alert.

## Sensitivity analyses

We conducted two sensitivity analyses. Given the central importance of the primary care relationship in the treatment of depression, we repeated the analysis among only the encounters between patients and their primary care provider. To assess whether the removal of providers with less than ten alert encounters over the entire study period incurred bias in the main analysis, the inclusion criteria were also relaxed to include them. Finally, physicians were trialed as fixed effects, with patients remaining as random effects, in order to remove unobserved heterogeneity between physicians.

Data extraction was performed in Microsoft SQL Server Management Studio 17. Statistical analyses and graphical representations were created using R Studio and JMP® software, respectively. Elixhauser comorbidity presence was computed in R using the *comorbidity* package. We considered the p-value of less than 0.05 to be statistically significant. This study was approved by the institutional review board of University of California, Los Angeles.

# RESULTS

During the three-and-a-half-year study period, there were a total of 55,649 encounters with associated depression screening alerts meeting the inclusion criteria (Supplementary Table 1). There were a total of 40,474 unique patients and 418 unique physicians.

## Physician characteristics

Two-thirds (66%) of the 418 physicians included in the study had graduated from medical school after 2000, and nearly half (44%) had graduated after 2010 (Supplementary Table 2). Female physicians made up a slightly larger proportion (58%). Nearly three-quarters (73%) of the physicians were internists or family practitioners. The median number of depression alerts seen by the physicians over the entire study period was 72 (interquartile range 28 to 179).

## Patient and encounter characteristics

Among the 55,649 encounters with depression alerts, nearly three-quarters (74%) were between patients and their primary care physician (Table 1). Approximately 90 percent of visits had a scheduled duration of thirty minutes or less. While the number of alerts increased between 2017 and 2019, the number of office visits with depression alerts decreased sharply after February 2020 (see Figure 2a), as expected due to the Covid-19 pandemic. Nearly two-thirds of

Table 1: Encounter, Physician and Patient Characteristics for Each Office Visits with an Accompanying Depression Alert*

| Characteristics | N=55,649 Encounters |
|---|---|
| Appointment with Patient's PCP[a], n (%) | |
| No | 14706 (26) |
| Yes | 40943 (74) |
| Appointment Length, n (%) | |
| 15 Minutes or Less | 21809 (39) |
| 20 to 30 Minutes | 27943 (50) |
| Greater than 30 Minutes | 5897 (11) |
| Encounter Year, n (%) | |
| 2017 | 2205 (4) |
| 2018 | 14127 (25) |
| 2019 | 21969 (39) |
| 2020 | 14759 (27) |
| 2021 | 2589 (5) |
| Competing BPA Alert Count, n (%) | |
| 0 | 21203 (38) |
| 1 | 22034 (40) |
| 2 | 9161 (16) |
| 3 or More | 3251 (6) |
| Provider Specialty, n (%) | |
| Family Medicine | 21635 (39) |
| Internal Medicine | 20617 (37) |
| Medicine-Pediatrics | 7657 (14) |
| Other | 757 (1) |
| Psychiatry | 4983 (9) |
| Provider Medical School Graduation Decade, n (%) | |
| 1980s or Earlier | 6364 (11) |
| 1990s | 13803 (25) |
| 2000s | 11589 (21) |
| 2010s | 23893 (43) |
| Number of Alerts Seen By Provider During Last 90 Days, n (%) | |
| < 125 | 13472 (24) |
| 125 - 333 | 13925 (25) |
| 334 - 720 | 14093 (25) |
| > 720 | 14159 (25) |
| Provider Sex, n (%) | |
| Female | 34479 (62) |
| Male | 21170 (38) |
| Patient Sex, n (%) | |
| Female | 36413 (65) |
| Male | 19236 (35) |
| Patient with Depression Active on Problem List, n (%) | |
| No | 50479 (91) |
| Yes | 5170 (9) |
| Patient with Antidepressant Rx in Last Year, n (%) | |
| No | 34063 (61) |
| Yes | 21586 (39) |
| Patient Age, median (IQR) | 42 (30, 59) |
| Patient PHQ-9, median (IQR) | 10 (7, 15) |
| Comorbidity Score[c], median (IQR) | -1 (-5, 2) |

* Percentages may not total 100 because of rounding. PHQ-9 denotes Patient Health Questionnaire-9, PCP Primary Care Provider, Rx Prescription.

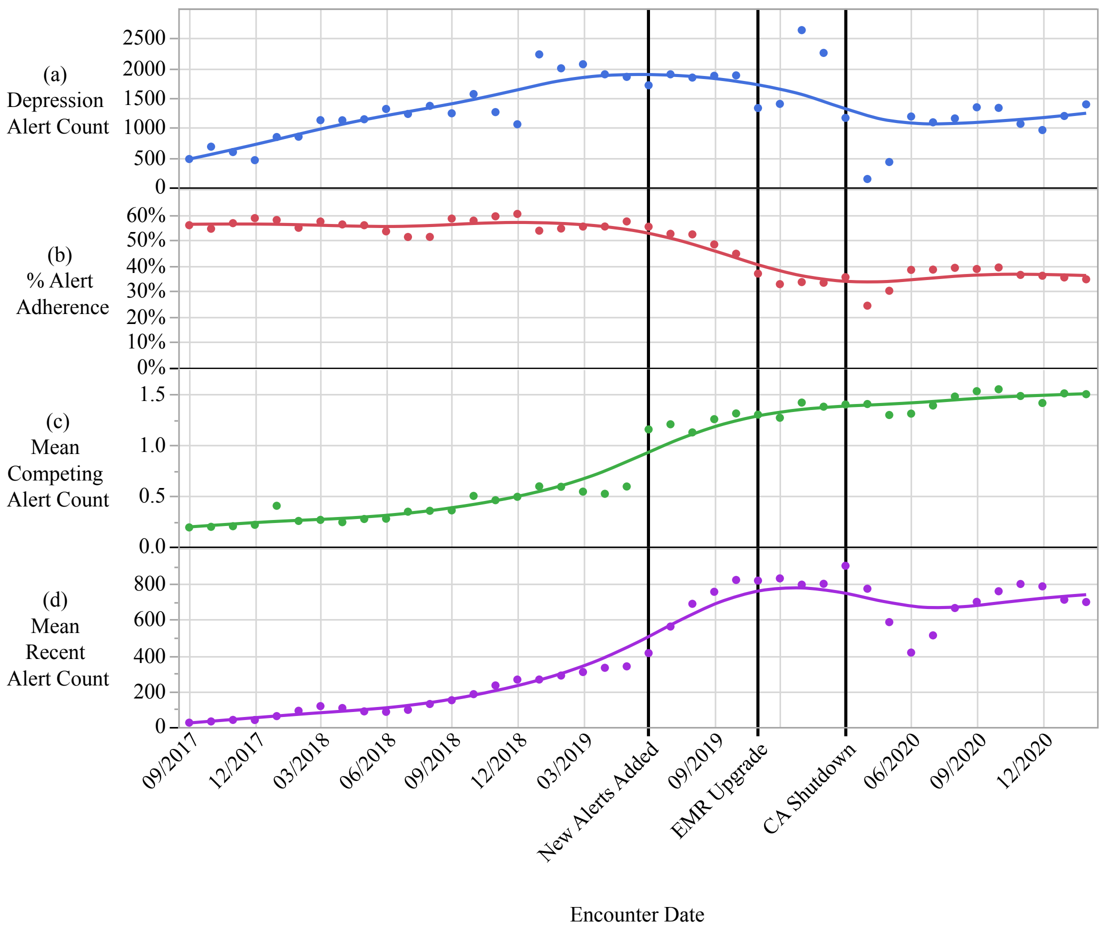
[a]Encounter provider is the patient's attributed primary care provider.

[b]*Other race* includes American Indian, Alaska Native, Native Hawaiian, other Pacific Islander, or race stated 'Other'

[c]AHRQ-weighted Elixhauser comorbidity score

visits were with female patients, and the median patient age was 42 (interquartile range 30-59). More than 90% of patients lacked an active depression diagnosis on their problem list at the time of their visit, and 61% had not received an antidepressant prescription over the preceding year.

Figure 2: Monthly Exposure and Response Rates for Depression Alerts




(a) Total number of encounters accompanied by depression alert per month. (b) Percent of depression alerts with uptake per month. (c) Average number of other clinical guidance alerts during each encounter with a depression alert. (d) Mean number of clinical guidance alerts (any) seen by encounter provider over the 90 days prior to the encounter. EHR denotes electronic health record, CA California

## Longitudinal Uptake Rates

The number of encounters with depression alerts (Figure 2a) increased steadily from September 2017 to May 2019. During this initial period, there was very little fluctuation in the monthly-average uptake of the depression alert (Figure 2b). However, June 2019 saw a stepwise increase in the average number of competing alerts appearing during the same encounter of each depression alert (Figure 2c). Following this change, the monthly-average uptake of the depression alert gradually decreased.

As expected, the monthly-average number of all alerts seen by physicians over the 90 days preceding each encounter (Figure 2d) began to increase accordingly. During this period, the upward trend of this lagging indicator mirrored the downward pattern of monthly average alert uptake. The overall decline in depression alert uptake clearly preceded two major systematic disruptions: a major EHR upgrade in November 2019 and the California Covid-19 Shutdown in March 2020.

## Modeling Alert Compliance

The median unadjusted depression alert uptake rate was 35% [IQR 7% to 72%]. The initial model utilized patient and physician random effects; however, given a substantially lower variance, the patient random effects were dropped from the final model for computational simplicity (Supplementary Table 3). The final model utilized physician random effects with adjustment for potential confounders (Table 2). The likelihood of alert uptake was higher among encounters with physicians in the second versus the first quartile of recent alert count (aOR 1.120; p=0.003). However, encounters with physicians in the higher quartiles of the recent alert count were much less likely to be accompanied by depression alert uptake (Q3 aOR 0.71, Q4 aOR 0.38; p<0.001 for both). In comparison to encounters with no competing alerts, encounters with one or more competing alerts were uniformly less likely to be followed by depression alert uptake. The lowest adjusted odds ratio was found in the encounters with three or more competing alerts compared to those with none at all (aOR 0.78; p<0.001).

Table 2: Generalized Linear Mixed-Effect Model of Depression Screen Alert Uptake*

| Covariate | Adjusted Probability of Alert Uptake[1] (95% CI) | Adjusted OR of PHQ-9 Alert Uptake (95% CI)[2] | p-value |
|---|---|---|---|
| **Provider Sex** | | | |
| Female | 33.9 (27.4-41.1) | Reference | |
| Male | 29.9 (22.9-38.0) | 0.833 (0.522-1.331) | 0.445 |
| **Alerts Seen by Provider in Last 90 Days[3]** | | | **<0.001†** |
| <125 (Q1) | 39.3 (33.7-45.2) | Reference | |
| 125 – 333 (Q2) | 42.0 (36.3-48.0) | 1.120 (1.039-1.208) | **0.003** |
| 334 – 720 (Q3) | 31.5 (26.5-36.9) | 0.709 (0.655-0.768) | **<0.001** |
| > 720 (Q4) | 19.8 (16.2-24.0) | 0.382 (0.350-0.417) | **<0.001** |
| **Competing Alerts During Encounter[4]** | | | **<0.001†** |
| 0 | 35.2 (29.9-40.9) | Reference | |
| 1 | 30.8 (26.0-36.2) | 0.822 (0.775-0.872) | **<0.001** |
| 2 | 30.6 (25.7-36.0) | 0.813 (0.753-0.879) | **<0.001** |
| 3 or More | 29.7 (24.6-35.3) | 0.778 (0.696-0.869) | **<0.001** |
| **Appointment With PCP[5]** | | | |
| No | 29.9 (25.1-35.2) | Reference | |
| Yes | 33.3 (28.2-38.8) | 1.170 (1.096-1.249) | **<0.001** |
| **Physician Specialty** | | | **<0.001†** |
| Internal Medicine | 35.2 (27.8-43.4) | Reference | |
| Family Medicine | 35.0 (26.3-45.0) | 0.993 (0.580-1.701) | 0.980 |
| Medicine-Pediatrics | 45.8 (28.6-64.0) | 1.554 (0.683-3.537) | 0.293 |
| Other | 11.5 (4.9-24.7) | 0.239 (0.089-0.645) | **0.005** |
| Psychiatry | 7.8 (4.0-14.2) | 0.156 (0.071-0.345) | **<0.001** |
| **MD Medical School Graduation Decade** | | | 0.538† |
| 1980s or Earlier | 31.6 (19.7-46.4) | Reference | |
| 1990s | 37.3 (26.4-49.7) | 1.290 (0.583-2.856) | 0.890 |
| 2000s | 26.6 (18.1-37.5) | 0.787 (0.351-1.762) | 0.569 |
| 2010s | 32.7 (25.5-40.7) | 1.052 (0.513-2.154) | 0.890 |
| **Patient Sex** | | | |
| Female | 31.7 (26.7-37.1) | Reference | |
| Male | 33.6 (28.5-39.2) | 1.092 (1.037-1.151) | **0.001** |
| **Patient with Active Depression Problem[6]** | | | |
| No | 33.0 (27.9-38.3) | Reference | |
| Yes | 26.5 (22.0-31.6) | 0.733 (0.678-0.793) | **<0.001** |
| **Patient Prescribed Antidepressant in Last Year** | | | |
| No | 33.5 (28.4-39.0) | Reference | |
| Yes | 30.6 (25.8-36.0) | 0.879 (0.836-0.924) | **<0.001** |
| **Patient PHQ-9 Score[7]** | - | 1.049 (1.044-1.054) | **<0.001** |
| **Patient Age[7]** | - | 0.996 (0.994-0.997) | **<0.001** |
| **AHRQ-weighted Elixhauser Comorbidity Score[7]** | - | 0.995 (0.992-0.998) | **<0.001** |

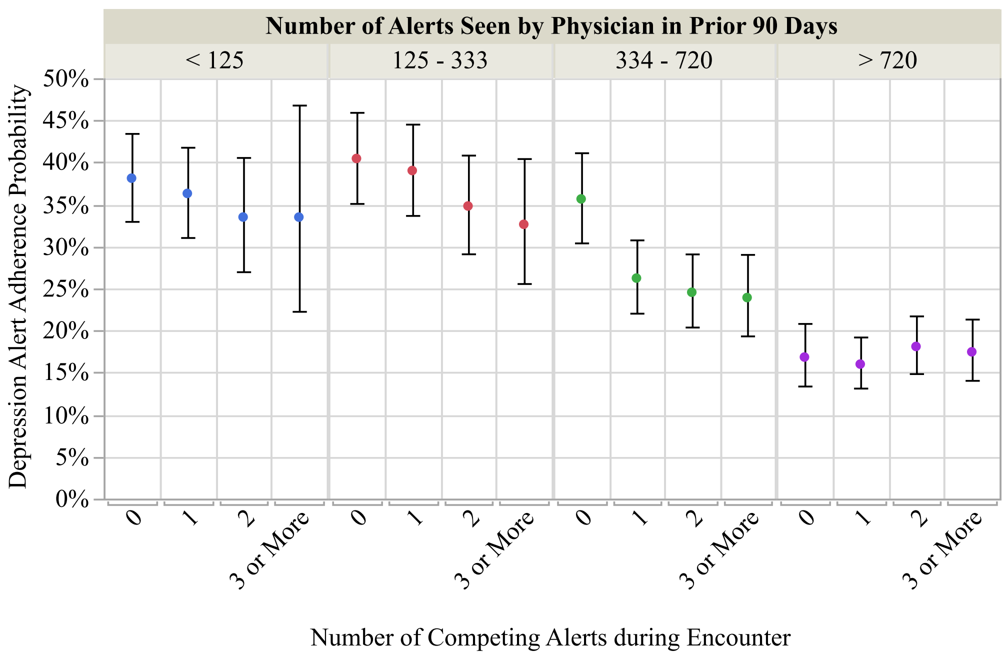
* The target outcome was positive uptake of the depression alert by the physician during the encounter. Patient race and ethnicity were trialed as model covariates but were not found to have statistical significance. OR denotes Odds Ratio, PCP Primary Care Physician, MD Medical Doctor, PHQ-9 Patient Health Questionnaire-9.

1. Calculated by marginal effects at the means (MEM).
2. Adjusted odds ratios from generalized mixed-effects modeling. Clustering performed at the level of individual physician with random effects.
3. Count of all clinical guidance alerts seen by the attending of record over the ninety days preceding the encounter.
4. Count of other clinical guidance alert (besides depression alert) seen by the attending during the encounter.
5. Primary care relationship between physician and patient on date of encounter.
6. Patient's problem list already contains one of the depression problems offered within the depression alert.
7. Unit odds ratio

† Overall significance of categorical variable assessed with ANOVA between model with and without variable

No difference was found between male or female physicians in terms of alert uptake. Similarly, the medical school graduation decade had no significant impact on alert uptake probability. However, the likelihood of alert uptake increased with the PHQ-9 value presented within the alert (unit aOR 1.05; p<0.001). The likelihood of alert uptake decreased with patient age (unit aOR 0.996; p<0.001) and patient comorbidity (unit aOR 0.995; p<0.001). Physicians seeing male patients versus female patients were more likely to utilize the depression alert (aOR 1.09; p<0.001).

Figure 3: Marginal Effect Plot of the Interaction Between Total Number of Alerts Seen by Provider over Past 90 Days and Number of Competing Alerts During Encounter




## Interaction of Recent Alert Count and Competing Alert Count

An interaction term between recent alert count and competing alert count was added to the first model. The addition of the interaction term resulted in better model fit (ANOVA p-value <0.001). In the first quartile of the recent alert count, the competing alert count did not significantly affect the adjusted probability of alert uptake (Figure 3). However, in the second quartile of recent alert exposure, the adjusted odds ratios of alert uptake were substantially lower with any competing alerts during the visit (aOR for ≥3 versus 0 competing alerts, 0.70; p=0.01). The same was true in the third quartile of recent alert exposure (aOR for ≥3 versus 0 competing alerts, 0.56; p<0.001). In the fourth quartile of recent alert exposure, there was no statistically significant difference in alert uptake between these levels (Supplemental Table 5).

### Sensitivity analyses

Our findings were qualitatively unaffected by restricting encounters to those between patients and their attributed primary care provider (Supplement Table 7). This was also true after including physicians who saw less than ten depression alerts during the study period (Supplemental Table 8). Treating as physicians as fixed effects resulted in no significant difference in the odds ratios of recent and competing alert counts on alert uptake (Supplementary Table 9).

## DISCUSSION

In the process of examining a gradual, yet persistent decline in depression screening alert uptake by physicians at a large academic health system, we found that physicians are less likely to respond to depression screening alerts when they had seen greater numbers of alerts recently. Depression screening alert uptake is also substantially diminished with competing alerts occurring in the same encounter; however interaction analysis reveals that this negative association only occurred during visits with physicians in the middle range of recent alert count. We also found that physicians are more likely to take up alerts for patients with higher depression severity scores, and less likely to take up alerts during encounters with older and more comorbid patients. This decrease in alert uptake is also true for patients having an active depression diagnosis already on the problem list and for those with a prescription for an antidepressant written in the preceding year.

It is reasonable to assume that major changes in alert uptake rates over time should occur in close approximation to the causal event. In the case of the decline in the use of the depression screening alert, we expected that the decline in alert uptake would have occurred after specific system-wide changes. However, our timeline showed that the decline happened before two expected drivers: (1) a major EHR system upgrade, and (2) the California Covid-19 shutdown, the latter being associated with shifts in office visit volume and workflow. Visualization of alert uptake over time did not reveal the decline to be stepwise, but rather, gradual over numerous months. To our knowledge, the relationship between changing healthcare system factors, such as the introduction of competing alerts, and individual alert performance has not been examined in this fashion. It is important to note that these findings indicate that declining uptake can manifest over an extended period of time after the inciting event, complicating both real-time detection of alert performance decay as well retrospective analyses to identify drivers of waning alert use. These findings should reiterate to vendors and administrators of EHR systems the criticality of long-term alert monitoring, an easily overlooked aspect of clinical decision support system management. This need will grow increasingly important as clinical decision support systems age with the dwindling presence of the original clinical stakeholders and alert designers.

We found an initial, slight improvement in depression screening alert uptake with increasing recent alert count, suggesting a sensitizing effect in this lower exposure range. However, for encounters with providers having a recent alert count above the median value, there was a dramatically reduced likelihood of depression screening alert uptake. Although a small number of studies have reported a lack of correlation between alert receipt frequency and acceptance rate [15, 24] there has been more evidence to support a negative relationship between alert exposure magnitude and uptake. A comprehensive analysis of both clinical guidance and drug-related alerts [18] demonstrated a marginally decreased likelihood of alert acceptance with increased exposure across an array of alert types. Interestingly, in that study, the sub-analysis of a depression-related alert did not find evidence of alert fatigue. In any case, the overall decrease in alert acceptance with receipt count, on an individual provider basis, was felt to be explained by either (1) alert fatigue or (2) a lesser need for clinical guidance among providers seeing the alert more often and therefore, more likely to be familiar with the management of the underlying disease. However, our findings are more consistent with alert fatigue, given an initial sensitization in alert uptake up to the second quartile of recent alert exposure, followed by a sharp decrease in the latter half.

Another study by the same group of researchers [12] provided further evidence that primary care physicians were less likely to accept alerts with an increasing receipt count. Although the number of unique alerts and overall alert counts was much higher than in the present study, there were noted to be many repeated alerts for the same patient in the same year. These findings were thought to support the conclusion that higher numbers of repetitive and uninformative alerts were associated with alert non-compliance. In a similar vein, our measure of recent alert exposure includes all alerts in the preceding 90 days, whether appropriate or not. However, our measured outcome is specific to physician uptake of a single, selective non-interruptive alert, appearing to the user due to a well-defined clinical trigger that is always accompanied by appropriate follow-up action. Our findings suggest that even appropriate alert usage might be deleteriously affected by high numbers of heterogeneous, mixed-quality alerts. Managers of clinical decision support systems should not consider the success of a newly implemented alert as durable, but rather, inherently dependent on the quality or volume of other EHR elements. Simplistic monitoring of alert performance over time should be supplemented with a suite of contextual, encounter-level metrics in order to better understand the overall environment in which alert performance may be degrading.

While the effect of competing alerts during a single visit was found to have a significantly negative impact on depression screening alert uptake, interaction analysis revealed that this effect was particular to encounters with physicians in the middle two quartiles of the recent alert count. That is, for encounters with physicians seeing very low or very high recent volumes of alerts, uptake was made no worse with an increasing number of competing alerts. At the low end, it is conceivable that these providers are less likely to be experiencing alert fatigue and potentially less susceptible to cognitive overload when presented with multiple competing alerts. At the high end of the recent alert count, alert fatigue may be driving a floor effect with depression alert uptake unaffected by the number of competing alerts. However, for encounters with providers in the middle two quartiles, the presence of any competing alerts substantially reduced the likelihood of depression alert uptake. These findings point to the potential benefit of orchestrating an adaptive "rationing" strategy, whereby low-priority alerts that may compete for a provider's attention could be withheld when doing so may improve alert uptake.

There was a strong association between the magnitude of the patient's depression score, which is shown at the top of the alert, and the likelihood of alert uptake. Prior studies of drug-drug interactions have shown that the probability of alert uptake may be directly related to the tiered risk presented within the alert[25, 26]. Our findings reinforce the notion that end-users respond dynamically to patient-specific, contextualizing information presented within alerts. To this end, designers of clinical decision support should aim to display any quantitative criteria driving alert firing. Provision of information regarding the severity of the underlying disorder can spotlight particularly serious cases and potentially overcome some of the deleterious effects of alert fatigue.

Our study has limitations. Encounters wherein non-attending staff was also exposed to the alert were excluded due to the difficulty in attributing follow-up responsibility. There may have been attending physicians, primarily based in resident clinics, for example, that were excluded for this reason. Additionally, in order to adjust for patient complexity, the AHRQ-weighted Elixhauser comorbidity score was calculated from all prior ICD-10 codes available in the EHR. Thus, where past medical history was not recorded or only documented in clinical notes, there was likely some inaccuracy of the comorbidity score.[27] Additionally, we analyzed the impact of overall alert exposure on only one non-interruptive alert, and it is possible that the impact may differ for other alerts. Finally, the physicians involved in the study were limited to those at a single academic medical center and therefore, the findings may not be generalizable to physicians at non-academic health care systems. Strengths of the study include the detailed, encounter-based modeling that accounted for particular features of each appointment and the long period of retrospective analysis.

In conclusion, we found that a successful depression alert was subtly, persistently, and negatively affected by the introduction of competing clinical guidance alerts and a concomitant rise in the overall number of alerts seen by physicians in the recent past. Health care systems should strive to actively monitor for declines in alert performance and for increases in overall alert exposure over extended periods of time. As changes and additions are made to the EHR on a continuous basis, diagnosing and treating underperforming clinical decision support systems requires the availability of tools that can provide a holistic understanding of the entire, dynamic EHR milieu.

# APPENDIX

Supplementary Table 1: Patient Flow

| | Patient Encounters |
|---|---|
| Unique Depression Alert Firings between 09/01/2017 – 02/28/2021 | 145,448 |
| Unique Patient Encounters with any Depression Alert Firings | 74,549 |
| Encounters with Alerts Received only by Attending Physicians | 66,780 |
| Encounters with Alert Fired At least Once on Day of Encounter | 62,859 |
| Encounters with Only One Attending Provider Receiving Alert | 62,645 |
| Completed Encounter Status | 62,482 |
| Attending Receiving Alert is Provider of Record | 61,455 |
| Encounter is Office Visit | 59,388 |
| Patient Sex: Male or Female | 59,383 |
| Patient Age >= 18 | 56,908 |
| Comorbidity Score able to be Calculated | 56,845 |
| Physician Graduation Year Available | 56,738 |
| Physician saw ten or more alerts during study period | 55,649 |

Supplementary Table 2: Characteristics of Unique Providers (N=418)

| | |
|---|---|
| Number of Alerts Seen over Study Period[a], Median (IQR) | 72 (28, 179) |
| Medical School Graduation Year Decade, N (%) | |
| 1980s or Earlier | 57 (14) |
| 1990s | 84 (20) |
| 2000s | 93 (22) |
| 2010s | 184 (44) |
| Provider Sex, N (%) | |
| Male | 175 (42) |
| Female | 243 (58) |
| Provider Specialty, N (%) | |
| Internal Medicine | 179 (43) |
| Family Medicine | 124 (30) |
| Medicine-Pediatrics | 38 (9) |
| Other[c] | 29 (7) |
| Psychiatry | 48 (11) |

a. Minimum 10, maximum 798

Supplementary Table 3: Initial Model with Both Patient and Physician Random Effects*

| Random Effect Group | N | Variance | Standard Deviation |
|---|---|---|---|
| Patient | 40474 | 0.095 | 0.308 |
| Physician | 418 | 5.340 | 2.311 |

| AIC | BIC | logLik | deviance | df.resid |
|---|---|---|---|---|
| 47807.4 | 48021.6 | -23879.7 | 47749.4 | 55625 |

| Covariate | Logit of Depression Alert Uptake[1] | p-value |
|---|---|---|
| **Provider Sex** | | |
| Female | Reference | |
| Male | -0.183 | 0.451 |
| **Alerts Seen by Provider in Last 90 Days[2]** | | |
| <125 (Q1) | Reference | |
| 125 – 333 (Q2) | -0.114 | **0.003** |
| 334 – 720 (Q3) | -0.456 | **<0.001** |
| > 720 (Q4) | -1.074 | **<0.001** |
| **Competing Alerts During Encounter[3]** | | |
| 0 | Reference | |
| 1 | -0.196 | **<0.001** |
| 2 | -0.205 | **<0.001** |
| 3 or More | -0.249 | **<0.001** |
| **Appointment With PCP** | | |
| No | Reference | |
| Yes | 0.158 | **<0.001** |
| **Physician Specialty** | | |
| Internal Medicine | Reference | |
| Family Medicine | -0.007 | 0.979 |
| Medicine-Pediatrics | 0.442 | 0.299 |
| Other | -1.434 | **0.005** |
| Psychiatry | -1.857 | **<0.001** |
| **MD Medical School Graduation Decade** | | |
| 1980s or Earlier | Reference | |
| 1990s | -0.048 | 0.898 |
| 2000s | -0.205 | 0.514 |
| 2010s | -0.292 | 0.350 |
| **Patient Sex** | | |
| Female | Reference | |
| Male | 0.088 | **0.001** |
| **Patient with Active Depression Problem[4]** | | |
| No | Reference | |
| Yes | -0.339 | **<0.001** |
| **Patient Prescribed Antidepressant in Last Year** | | |
| No | Reference | |
| Yes | -0.128 | **<0.001** |
| **Patient PHQ-9 Score[5]** | 0.048 | **<0.001** |
| **Patient Age[5]** | -0.004 | **<0.001** |
| **AHRQ-weighted Elixhauser Comorbidity Score[5]** | -0.005 | **<0.001** |

*The target outcome was positive uptake of the depression alert by the physician during the encounter. Patient race and ethnicity were trialed as model covariates but were not found to have statistical significance. 55,649 encounters, 40474 patients, 418 physicians. OR Odds Ratio, PCP Primary Care Physician, MD Medical Doctor.

1. Adjusted odds ratios from generalized mixed-effects modeling. Clustering performed at the level of individual physician and patient with random effects.
2. Count of all clinical guidance alerts seen by the attending of record over the ninety days preceding the encounter.
3. Count of other clinical guidance alerts (besides depression alert) seen by the attending during the encounter.
4. Patient's problem list already contains one of the depression problems offered within the depression alert.
5. Unit odds ratio

Supplementary Table 4: ANOVA Test Comparing Base Model and Interaction Model*

| Model | Df | AIC | BIC | logLik | Deviance | Chisq | Chi Df | p-value |
|---|---|---|---|---|---|---|---|---|
| Main model | 23 | 47815 | 48020 | -23855 | 47769 | | | |
| Interaction model | 32 | 47771 | 48057 | -23854 | 47707 | 61.932 | 9 | <0.001 |

*Main model and interaction model adjust for physician factors (number of alerts seen in previous 90 days, graduation year decade, specialty, PCP status with patient), patient factors (age, PHQ-9 score, Elixhauser comorbidity score, depression diagnosis active on problem list, prescription for antidepressant in past year) and encounter factors (number of competing alerts). Physician is used as the single random effect.

Supplementary Table 5: Interaction Model with Stratification by Recent Alert Exposure

| Recent Alert Exposure | Competing Alert Count | Adjusted OR of PHQ-9 Alert Uptake (95% CI)[2] | p-value |
|---|---|---|---|
| <125 (Q1) | 0 | Reference | |
| | 1 | 0.912 (0.813-1.022) | 0.132 |
| | 2 | 0.817 (0.641-1.041) | 0.103 |
| | 3 or More | 0.883 (0.500-1.558) | 0.667 |
| 125 – 333 (Q2) | 0 | Reference | |
| | 1 | 0.940 (0.847-1.044) | 0.249 |
| | 2 | 0.781 (0.663-0.921) | **0.003** |
| | 3 or More | 0.695 (0.527-0.917) | **0.010** |
| 334 – 720 (Q3) | 0 | Reference | |
| | 1 | 0.642 (0.574-0.718) | **<0.001** |
| | 2 | 0.587 (0.514-0.669) | **<0.001** |
| | 3 or More | 0.564 (0.470-0.678) | **<0.001** |
| > 720 (Q4) | 0 | Reference | |
| | 1 | 0.949 (0.807-1.116) | 0.529 |
| | 2 | 1.101 (0.928-1.306) | 0.270 |
| | 3 or More | 1.053 (0.862-1.286) | 0.614 |

Supplementary Table 6: Interaction Model with Stratification by Competing Alert Count

| Competing Alert Count | Recent Alert Exposure | Adjusted OR of PHQ-9 Alert Uptake (95% CI)[2] | p-value |
|---|---|---|---|
| 0 | <125 (Q1) | Reference | |
| | 125 – 333 (Q2) | 1.106 (1.007-1.216) | **0.036** |
| | 334 – 720 (Q3) | 0.899 (0.802-1.008) | 0.068 |
| | > 720 (Q4) | 0.325 (0.275-0.385) | **<0.001** |
| 1 | <125 (Q1) | Reference | |
| | 125 – 333 (Q2) | 1.141 (1.004-1.297) | **0.043** |
| | 334 – 720 (Q3) | 0.633 (0.560-0.715) | **<0.001** |
| | > 720 (Q4) | 0.339 (0.300-0.382) | **<0.001** |
| 2 | <125 (Q1) | Reference | |
| | 125 – 333 (Q2) | 1.058 (0.802-1.394) | 0.690 |
| | 334 – 720 (Q3) | 0.645 (0.501-0.832) | **<0.001** |
| | > 720 (Q4) | 0.438 (0.341-0.563) | **<0.001** |
| 3 or More | <125 (Q1) | Reference | |
| | 125 – 333 (Q2) | 0.871 (0.467-1.623) | 0.664 |
| | 334 – 720 (Q3) | 0.574 (0.320-1.032) | 0.064 |
| | > 720 (Q4) | 0.388 (0.217-0.692) | **0.001** |

Supplementary Table 7: Sensitivity Analysis Including only Encounters between Patients and their Primary Care Providers*

| Covariate | Adjusted OR of Depression Alert Uptake (95% CI)[1] | p-value |
|---|---|---|
| **Provider Sex** | | |
| Female | Reference | |
| Male | 0.722 (0.446-1.17) | 0.186 |
| **Alerts Seen by Provider in Last 90 Days[2]** | | |
| <125 (Q1) | Reference | |
| 125 – 333 (Q2) | 1.149 (1.053-1.254) | **0.002** |
| 334 – 720 (Q3) | 0.739 (0.674-0.809) | **<0.001** |
| > 720 (Q4) | 0.398 (0.361-0.439) | **<0.001** |
| **Competing Alerts During Encounter[3]** | | |
| 0 | Reference | |
| 1 | 0.778 (0.727-0.832) | **<0.001** |
| 2 | 0.786 (0.72-0.857) | **<0.001** |
| 3 or More | 0.726 (0.642-0.82) | **<0.001** |
| **Physician Specialty** | | |
| Internal Medicine | Reference | |
| Family Medicine | 1.098 (0.659-1.831) | 0.720 |
| Medicine-Pediatrics | 1.375 (0.639-2.959) | 0.416 |
| Other | 1.332 (0.278-6.379) | 0.720 |
| Psychiatry | 1.089 (0.117-10.187) | 0.940 |
| **MD Medical School Graduation Decade** | | |
| 1980s or Earlier | Reference | |
| 1990s | 1.555 (0.814-2.970) | 0.225 |
| 2000s | 1.060 (0.463-2.423) | 0.891 |
| 2010s | 1.461 (0.717-2.976) | 0.296 |
| **Patient Sex** | | |
| Female | Reference | |
| Male | 1.096 (1.033-1.164) | **0.002** |
| **Patient with Active Depression Problem[4]** | | |
| No | Reference | |
| Yes | 0.712 (0.653-0.776) | **<0.001** |
| **Patient Prescribed Antidepressant in Last Year** | | |
| No | Reference | |
| Yes | 0.894 (0.845-0.946) | **<0.001** |
| **Patient PHQ-9 Score[5]** | 1.049 (1.043-1.054) | **<0.001** |
| **Patient Age[5]** | 0.996 (0.995-0.998) | **<0.001** |
| **AHRQ-weighted Elixhauser Comorbidity Score[5]** | 0.995 (0.991-0.998) | **<0.001** |

* The target outcome was positive uptake of the depression alert by the physician during the encounter. Patient race and ethnicity were trialed as model covariates but were not found to have statistical significance. 40,943 encounters, 344 physicians, 31,251 patients. OR Odds Ratio, PCP Primary Care Physician, MD Medical Doctor.

1. Adjusted odds ratios from generalized mixed-effects modeling. Clustering performed at the level of individual physician and patient with random effects.
2. Count of all clinical guidance alerts seen by the attending of record over the ninety days preceding the encounter.
3. Count of other clinical guidance alerts (besides depression alert) seen by the attending during the encounter.
4. Patient's problem list already contains one of the depression problems offered within the depression alert.
5. Unit odds ratio

Supplementary Table 8: Sensitivity Analysis without Minimum Number of Alert Encounters for Physicians*

| Covariate | Adjusted OR of Alert Uptake (95% CI)[1] | p-value |
|---|---|---|
| **Provider Sex** | | |
| Female | Reference | |
| Male | 0.658 (0.445-0.972) | **0.036** |
| **Alerts Seen by Provider in Last 90 Days[2]** | | |
| < 259 (Q1) | Reference | |
| 259 – 521 (Q2) | 1.126 (1.039-1.220) | **0.004** |
| 522 – 934 (Q3) | 0.792 (0.727-0.863) | **<0.001** |
| > 934 (Q4) | 0.439 (0.400-0.482) | **<0.001** |
| **Competing Alerts During Encounter[3]** | | |
| 0 | Reference | |
| 1 | 0.763 (0.720-0.809) | **<0.001** |
| 2 | 0.729 (0.676-0.787) | **<0.001** |
| 3 or More | 0.687 (0.616-0.767) | **<0.001** |
| **Appointment With PCP** | | |
| No | Reference | |
| Yes | 1.175 (1.101-1.255) | **<0.001** |
| **Physician Specialty** | | |
| Internal Medicine | Reference | |
| Family Medicine | 1.010 (0.619-1.648) | 0.967 |
| Medicine-Pediatrics | 1.736 (0.791-3.810) | 0.169 |
| Other | 0.199 (0.118-0.336) | **<0.001** |
| Psychiatry | 0.229 (0.111-0.473) | **<0.001** |
| **MD Medical School Graduation Decade** | | |
| 1980s or Earlier | Reference | |
| 1990s | 1.555 (0.814-2.970) | 0.181 |
| 2000s | 0.719 (0.381-1.358) | 0.309 |
| 2010s | 1.091 (0.610-1.951) | 0.769 |
| **Patient Sex** | | |
| Female | Reference | |
| Male | 1.091 (1.036-1.150) | **0.001** |
| **Patient with Active Depression Problem[4]** | | |
| No | Reference | |
| Yes | 0.705 (0.652-0.763) | **<0.001** |
| **Patient Prescribed Antidepressant in Last Year** | | |
| No | Reference | |
| Yes | 0.881 (0.838-0.926) | **<0.001** |
| **Patient PHQ-9 Score[5]** | 1.051 (1.046-1.056) | **<0.001** |
| **Patient Age[5]** | 0.996 (0.995-0.998) | **<0.001** |
| **AHRQ-weighted Elixhauser Comorbidity Score[5]** | 0.995 (0.992-0.998) | **<0.001** |

* The target outcome was positive uptake of the depression alert by the physician during the encounter. Patient race and ethnicity were trialed as model covariates but were not found to have statistical significance. 56,738 encounters, 780 physicians, 41,342 patients. OR Odds Ratio, PCP Primary Care Physician, MD Medical Doctor

1. Adjusted odds ratios from generalized mixed-effects modeling. Clustering performed at the level of individual physician and patient with random effects.
2. Count of all clinical guidance alerts seen by the attending of record over the ninety days preceding the encounter.
3. Count of other clinical guidance alerts (besides depression alert) seen by the attending during the encounter.
4. Patient's problem list already contains one of the depression problems offered within the depression alert.
5. Unit odds ratio

Supplementary Table 9: Physicians as Fixed Effects*

| Covariate | Adjusted OR of Alert Uptake (95% CI)[1] | p-value |
|---|---|---|
| **Provider Sex** | | |
| Female | Reference | |
| Male | 0.541 (0.051 – 5.733) | 0.610 |
| **Alerts Seen by Provider in Last 90 Days[2]** | | |
| < 125 (Q1) | Reference | |
| 125 – 332 (Q2) | 1.130 (1.046 – 1.220) | 0.002 |
| 333 – 720 (Q3) | 0.711 (0.655 – 0.772) | <0.001 |
| > 720 (Q4) | 0.382 (0.349 – 0.417) | <0.001 |
| **Competing Alerts During Encounter[3]** | | |
| 0 | Reference | |
| 1 | 0.822 (0.774 – 0.873) | <0.001 |
| 2 | 0.815 (0.753 – 0.882) | <0.001 |
| 3 or More | 0.780 (0.696 – 0.874) | <0.001 |
| **Appointment With PCP** | | |
| No | Reference | |
| Yes | 1.168 (1.093 – 1.249) | <0.001 |
| **Physician Specialty** | | |
| Internal Medicine | Reference | |
| Family Medicine | 0.084 (0.021 – 0.345) | <0.001 |
| Medicine-Pediatrics | 3.314 (0.253 – 43.380) | 0.361 |
| Other | 0.098 (0.014 – 0.678) | 0.019 |
| Psychiatry | 0.134 (0.012 – 1.604) | 0.113 |
| **MD Medical School Graduation Decade** | | |
| 1980s or Earlier | Reference | |
| 1990s | 396.888 (16.844 – 9351.548) | <0.001 |
| 2000s | 77.318 (5.117 – 1168.231) | 0.002 |
| 2010s | 24.481 (2.864 – 209.264) | 0.003 |
| **Patient Sex** | | |
| Female | Reference | |
| Male | 1.092 (1.036 – 1.152) | 0.001 |
| **Patient with Active Depression Problem[4]** | | |
| No | Reference | |
| Yes | 0.704 (0.651 – 0.763) | <0.001 |
| **Patient Prescribed Antidepressant in Last Year** | | |
| No | Reference | |
| Yes | 0.879 (0.835 – 0.925) | <0.001 |
| **Patient PHQ-9 Score[5]** | 1.050 (1.045 – 1.055) | <0.001 |
| **Patient Age[5]** | 0.996 (0.994 – 0.997) | <0.001 |
| **AHRQ-weighted Elixhauser Comorbidity Score[5]** | 0.995 (0.992 – 9.998) | <0.001 |

* The target outcome was positive uptake of the depression alert by the physician during the encounter. Patient race and ethnicity were trialed as model covariates but were not found to have statistical significance. OR Odds Ratio, PCP Primary Care Physician, MD Medical Doctor

1. Adjusted odds ratios from generalized mixed-effects modeling. Clustering performed at the level of individual patient with physicians treated as fixed effects.
2. Count of all clinical guidance alerts seen by the attending of record over the ninety days preceding the encounter.
3. Count of other clinical guidance alerts (besides depression alert) seen by the attending during the encounter.
4. Patient's problem list already contains one of the depression problems offered within the depression alert.
5. Unit odds ratio

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