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Diagnostic Trajectories in Primary Care at 12 Months: An Observational Cohort Study

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Background: Little is known about the epidemiology of diagnosis in primary care.

Methods: A prospective observational cohort study was conducted of adults presenting between August and December 2018 to primary care clinics across two health systems with an undiagnosed medical problem. Primary outcomes were (1) likelihood of a definitive diagnosis by 12 months and (2) time to diagnosis. Multivariate logistic regression was used to assess for factors associated with the likelihood of reaching a diagnosis, and multivariable Cox regression was used to assess for factors associated with time to diagnosis. Bivariate models were used to explore unadjusted relationships between the cases' organ systems and likelihood of and time to diagnosis.

Results: Among 410 cases in a diverse patient population, 206 (50.2%) reached a final diagnosis within 12 months, with a median time to diagnosis of 5 days (interquartile range = 0–46). Among these cases, 32.4% reached a diagnosis within the first month. A majority of cases not diagnosed within a month of the first presentation remained undiagnosed at 12 months. The likelihood of diagnosis and time to diagnosis did not differ by clinician or patient characteristics, clinicians' level of diagnostic uncertainty, chronicity of the medical issue, or visit type. There were no significant associations between organ system and likelihood of time to diagnosis.

Conclusion: Patients presenting with new or unresolved problems in ambulatory primary care often remain undiagnosed after a year. There were no provider or patient-level variables associated with such lack of diagnosis. The causes, contributors, and consequences of lack of timely diagnosis and potential solutions require further research.

There is growing concern about diagnostic error (defined as missed, delayed, or wrong diagnoses) in primary care as a significant public health concern,[1] with an estimated 5% of adults in the United States experiencing a diagnostic error in the outpatient setting every year.[2,3] Addressing this issue has proven intractable, in part because *diagnostic error* is difficult to define and measure. For example, many patient safety experts wonder whether a missed diagnosis that doesn't cause harm should be considered an error. However, the goal of medical care is not simply to avoid errors. Making a correct and timely diagnosis is imperative to the provision of safe patient care and central to the practice of primary care medicine.[3]

To date, no prospective study has characterized how often or how quickly primary care clinicians typically reach a final diagnosis for the cases they encounter in clinic. This knowledge gap is critical because many patients begin their diagnostic journey in the primary care setting, and potential delays or errors in primary care can prevent patients from receiving necessary subspecialty care, diagnostic tests, or procedures and treatments that require a referral from primary care. Thus, primary care diagnostic performance influences many other health care settings. Moreover, the primary care environment is cognitively challenging, with time pressure[4] and frequent interruptions,[5] both of which impede the cognitive work of making a diagnosis.[6,7] Understanding how diagnosis unfolds in primary care is critical to the development, testing, and evaluation of interventions to improve diagnosis.

To address this knowledge gap, we examined the electronic medical record data of adult patients presenting to primary care providers across two health systems with a medical complaint/issue not yet diagnosed to determine the likelihood of having an established final diagnosis within 12 months and the median time to have a final diagnosis. We then assessed patient, clinician, and case factors that might be associated with these diagnostic outcomes.

METHODS

We conducted a longitudinal prospective observational cohort study of patients who presented to primary care clinics with a medical complaint or issue that was not yet diagnosed.

Study Population

The study population consisted of adult patients (aged ≥ 18 years) who made at least one visit during a pragmatic

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randomized controlled trial (RCT) (between August and December of 2018) to 1 of 28 participating primary care providers (PCPs) across two health systems in San Francisco, who received peer consultation via an online digital technology platform to assist in their diagnosis of randomly selected cases that did not yet have an established, confirmed diagnosis. The RCT intervention involved the provision of peer opinions on the differential diagnosis and diagnostic steps. Physician scribes, who were primary care clinicians in the same health care system as participating PCPs, entered one-line summaries with relevant history, exams, and tests onto a digital platform (the Human Diagnosis Project [Human Dx]; Human Dx, San Francisco). This platform allows clinicians to submit a clinical case to elicit feedback on the diagnosis and plan as well as to provide feedback on submitted cases. Using Human Dx, we solicited opinions about diagnoses and next steps from an online community of US–based attending internists or family medicine physicians who had solved one Human Dx case in the past 3 months. Providers either practice at the city- and county-funded, safety-net integrated health system, which sees low-income, racially, ethnically, and linguistically diverse populations, or at one of several primary care sites within a large tertiary academic medical center. The academic medical center has a wide range of patients with respect to race/ethnicity, income, and educational attainment and accepts public and private insurance. These providers had participated in a pragmatic RCT of a digital platform that provided peer input to help providers make diagnostic decisions on clinical cases that did not yet have an established, confirmed diagnosis. The protocol and primary findings of the trial have been previously reported.[8,9]

Case Inclusion Criteria

Our unit of analysis was primary care clinic encounters, which we refer to as "cases," with potential diagnostic uncertainty. Physician adjudicators, not the treating PCPs, reviewed completed notes from primary care encounters within 72 hours to determine which cases to include in the study (Figure 1). The physician adjudicators applied criteria from the literature[10] to identify encounters with potential diagnostic uncertainty. Cases were included if they met one of five possible inclusion criteria: (1) new symptom or test abnormality, (2) unresolved symptom or test abnormality without a definitive etiology, (3) test ordered to assess an unresolved concern, (4) empiric treatment documented for the undiagnosed symptom or test abnormality, or (5) specialist referral for diagnostic assistance. The physician adjudicators abstracted the date, patient medical record number, and pertinent clinical details at the time of the initial encounter.

Chart Review for Ascertainment and Adjudication of Outcomes and Covariates

Subsequently, physician adjudicators independently reviewed the cases using the electronic health record (EHR) 12 months after the initial encounter to ascertain the final diagnosis (via clinicians' documentation, laboratory results, imaging or procedure reports, specialist consultant notes, or other–not specified) and adjudicate the status of cases that did not reach a definitive diagnosis (Figures 2 and 3). A study investigator reviewed initial adjudication results (5–15 cases) across all adjudicators to ensure accuracy and consistency of adjudication results. Any disagreements were reconciled through discussion until a consensus was made.

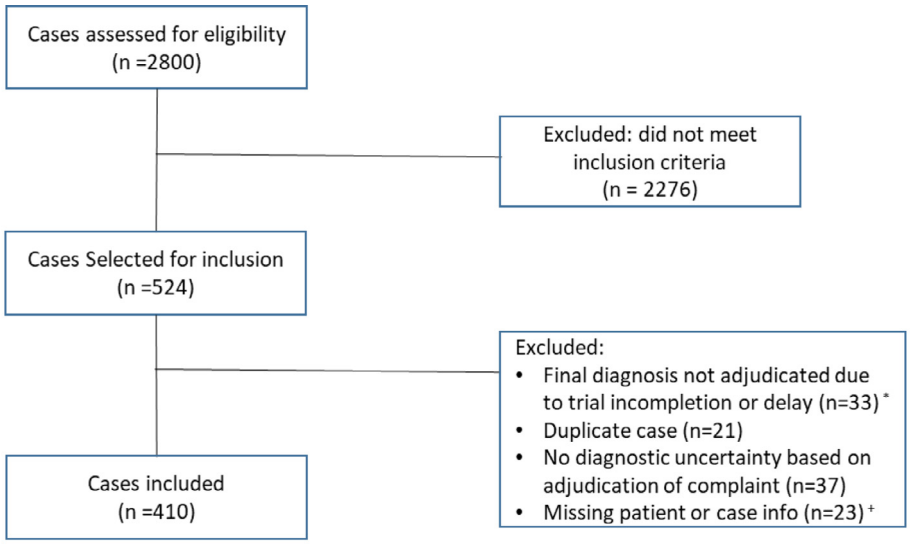
To ascertain the types of clinical cases in our cohort, two study investigators independently reviewed the one-line case summaries entered by the physician scribes and classified cases into organ systems using an ICD-10 classification scheme,[11] including heme, neoplasm, endocrine, metabolic, mental, and behavioral disorders; nervous system; diseases of the eye and adnexa; diseases of the ear and mastoid process; circulatory; respiratory; digestive; skin and subcutaneous tissue; musculoskeletal; genitourinary; obstetrics; abnormal signs, symptoms, labs, or imaging; and injury or poison. The investigators met to reconcile disagreements to reach a consensus for all cases; the cases were finalized only when the two investigators agreed on the organ system.

Outcomes

Our primary outcomes of interest were (1) the likelihood of having a definitive diagnosis by 12 months and, (2) among diagnosed cases, the time it took to reach a diagnosis. Time to diagnosis was defined as the interval between the date of the clinic visit from which a case was identified and the adjudicated date of having a definitive diagnosis based on EHR chart review. Time to diagnosis could not be calculated for those cases that remained undiagnosed.

Covariates

Primary care providers self-reported selected characteristics (clinical specialty or training [family medicine vs. internal medicine vs. nurse practitioner] and years in practice) at baseline. In addition, case-level surveys were sent to providers weekly for them to rate the (1) level of difficulty of the case (not at all or somewhat vs. moderate or high), and (2) diagnostic uncertainty of the case (not at all or somewhat vs. moderate or high). Patient characteristics (gender, race or ethnicity, age), number of comorbidities (using the Elixhauser index[12] to categorize and count comorbidities), chronicity of medical issue (new, less than 6 months, or more than 6 months), and type of visit (new, returning, or drop-in) were collected through chart review.



* We do not have adjudication data for these cases because as per trial protocol, cases originally randomized to the peer-input intervention that did not receive peer input from at least 3 contributors were not adjudicated for final diagnosis and time to diagnosis.
+ Cases for which we either could not find the patient presumably because the medical record number recorded in our dataset was wrong or that the data in the medical record did not corresponding to the case details in our dataset.

Figure 1: The CONSORT (Consolidated Standards of Reporting Trials) diagram illustrates our case selection and inclusion process.

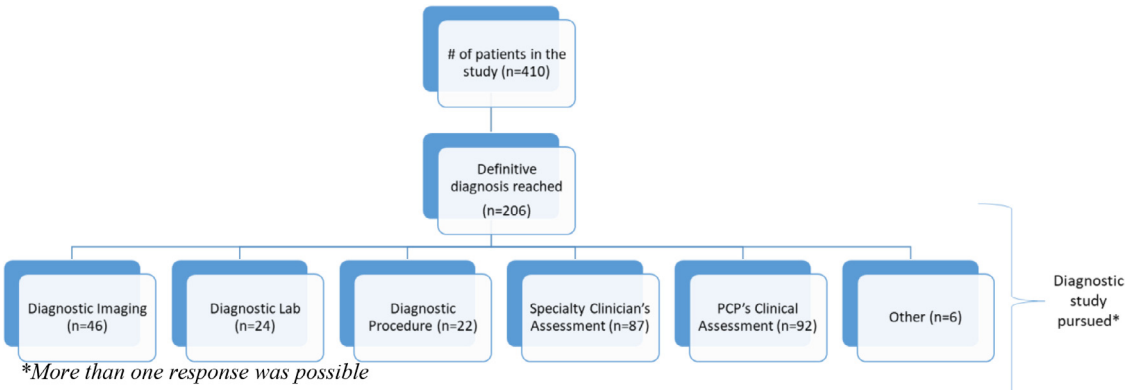


Figure 2: Shown here is the diagnostic trajectory of cases that reached a diagnosis at 12 months. To ascertain the final diagnosis, physician adjudicators were instructed to review the electronic patient chart, including clinicians' notes, laboratory results, diagnostic imaging, and procedures and referrals, and report whether the final diagnosis was reached via diagnostic imaging, diagnostic lab, diagnostic procedure, specialist clinician's assessment, PCP's clinical assessment, or other. "Other" was not specified. PCP, primary care provider.

Statistical Analysis

Because the digital peer consultation platform did not change the outcomes of interest described above, we pooled the intervention and control-group cases from the trial for this observational data analysis. We report the proportion of cases that reached a definitive diagnosis within 12 months of initial presentation and used an unadjusted Cox regression analysis to describe the time to diagnosis. In keeping with an intention-to-treat approach, our analysis included cases in which patients did not have a follow-up visit within our study period (see Table 1). Cases for which we could not adjudicate the outcome variables were excluded; cases originally randomized to the peer-input intervention (described above) that did not receive peer input from at least three contributors were not adjudicated for final diagnosis, as per trial protocol. We used a multivariate logistic regression to assess for factors associated with the likelihood of reaching a diagnosis within 12 months and a multivariable Cox regression to assess for factors associated with time to diagnosis. Covariates in the regression models were chosen a priori based on clinical judgment to include PCP characteristic (type of training and number of years in practice), clinical case factors (single vs. multiple chief complaints, perceived level of difficulty, the baseline level of diagnostics uncer-

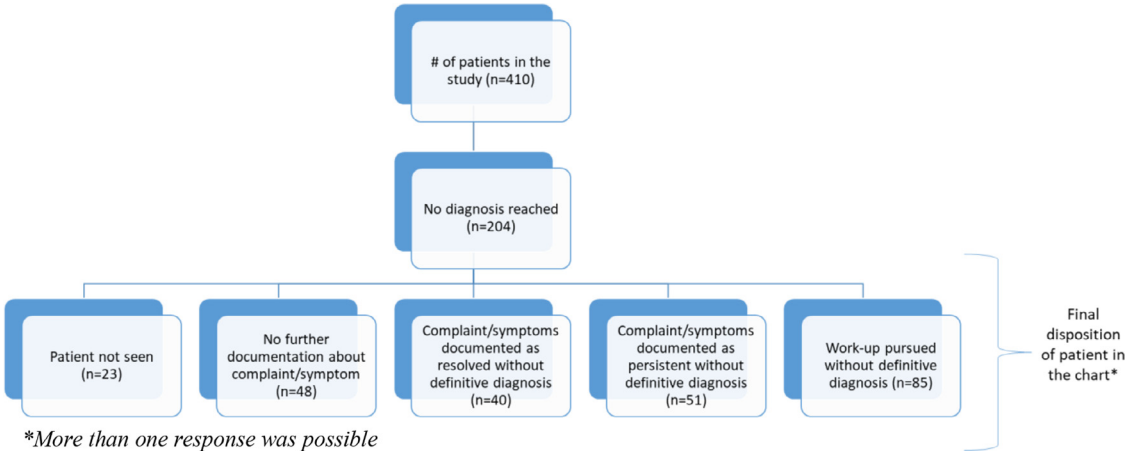


Figure 3: The graph shows the diagnostic trajectory of cases that did not reach a diagnosis at 12 months. For cases without a final diagnosis, physician adjudicators were instructed to ascribe the final disposition into five categories (listed in the figure) based on their chart review.

Table 1. Adjudication of Final Diagnosis at 12 Months Among Cases with Diagnostic Uncertainty at Baseline (Aug. to Nov. 2018)

Definitive diagnosis reached via . . .	***N* = 206 (%)**
PCP's documentation of clinical assessment	92 (44.7)
Diagnostic imaging report	46 (22.3)
Diagnostic laboratory results	24 (11.7)
Diagnostic procedure report	22 (10.7)
Note from specialist consultant	87 (42.2)
Other	6 (2.9)
No definitive diagnosis reached at 12 months	***N* = 204 (%)**
Patient not seen after index visit	23 (11.3)
No further documentation about the complaint	48 (23.5)
Complaint documented as resolved without definitive diagnosis	40 (19.6)
Complaint documented as persistent without definitive diagnosis	51 (25.0)
Workup pursued but no definitive diagnosis was reached	85 (41.7)

PCP, primary care provider.

tainty, and chronicity of the medical issue), patient demographic characteristics (age, gender, and race) and type of visit (new, returning, or drop-in) and health system (safety-net health system vs. academic medical center). Given our limited sample size, we performed separate bivariate models (logistic and Cox regression) as an exploratory analysis to examine the potential association between the chief complaint's organ system classification and the likelihood and time to diagnosis (Appendix Table 1, available in online article).

RESULTS

Among patients who made at least one visit to 1 of 28 participating clinicians during our enrollment period between August and December of 2018 (Figure 1), we assessed 2,800 visits and identified 524 potential cases (with a new or unresolved complaint) for study inclusion. We excluded 114 cases that were adjudicated not to have a diagnostic uncertainty at baseline or that had incomplete adjudication data, yielding a final cohort of 410 patients contributing cases for our analysis with a variety of complaints or unresolved medical issues associated with various organ systems, most commonly digestive (17.3%), musculoskeletal (14.7%), and skin (15.2%). The most common method of reaching a diagnosis was a clinical assessment by the PCP (44.7%) or assessment by a specialty consulting clinician (42.2%) (Table 1). The final status or disposition for cases that did not have a diagnosis included patients not seen after the index visit (11.3%) and complaints that resolved without definitive diagnosis (19.6%) (Table 1). The majority of the remaining cases had a workup pursued without detecting a final diagnosis (85 out of 141).

The study population had a mean age of 53.4 years, and 242 (59.0%) were female (Table 2). There was a diverse population of patients: 14.9% Black ($n = 61$), 16.1% White ($n = 66$), 33.7% Hispanic ($n = 138$), and 27.6% Asian ($n = 113$). There was no demographic difference (age, gender, race) between patients (Appendix Table 2). Overall, 24.9% of cases (102/410) were perceived as moderately or very difficult by the clinicians, and they reported moderate or high-level diagnostic uncertainty for 24.1%

Table 2. Description of Participating Clinicians and Cases with Diagnostic Uncertainty

Clinician Characteristics ($N = 28$)	
Clinician training or specialty, *n* (%)*	
Internal Medicine	14 (50.0)
Family Medicine	6 (21.4)
Nurse Practitioner	8 (28.6)
Years in practice, *n* (%)	
< 5 years	10 (35.7)
5–9 years	5 (17.9)
10–20 years	8 (28.6)
> 20 years	5 (17.9)
Patient Characteristics ($N = 410$)	
Patient age in years, mean (SD)	53.4 (16.4)
18–34 (%)	55 (13.4)
35–49 (%)	108 (26.3)
50–64 (%)	141 (34.4)
65–74 (%)	69 (16.8)
≥ 7+ (%)	35 (8.5)
Gender, *n* (%)	
Female	242 (59.0)
Male	168 (41.0)
Race/Ethnicity, *n* (%)	
Non-Hispanic Black	61 (14.9)
Non-Hispanic White	66 (16.1)
Hispanic	138 (33.7)
Asian	113 (27.6)
Other	25 (6.1)
Number of comorbid conditions, mean (SD)	0.6 (1.4)
Case-Related Factors ($N = 410$)	
Chief complaints	
Single chief complaint	351 (85.6)
Multiple chief complaints	59 (14.4)
Perceived level of difficulty, *n* (%)	
Not at all or somewhat difficult	300 (73.2)
Moderately or very difficult	102 (24.9)
Clinician's baseline level of diagnostic uncertainty, *n* (%)	
Not at all or somewhat uncertain	306 (74.6)
Moderately or very uncertain	99 (24.1)
Chronicity of medical issue, *n* (%)	
New medical issue	319 (77.8)
Ongoing for 3–6 months	42 (10.2)
Ongoing for 6 months or more	41 (10.0)
Type of visit, *n* (%)	
New	35 (8.5)
Returning	267 (65.1)
Drop-in	69 (16.8)
Other	26 (6.3)

* The percentages are presented as column percentage.

of cases. New medical issues or complaints accounted for 77.8% of cases ($n = 319$), while 10.2% ($n = 42$) were ongoing for 3 to 6 months, and 10.0% ($n = 41$) were ongoing for more than 6 months. Only 8.5% of cases ($n = 35$) occurred at a new patient visit vs. 65.1% returning ($n = 267$) vs. 16.8% drop-in visit ($n = 69$).

In our sample, 50.2% of cases reached a final diagnosis within 12 months ($n = 206$), with a median time to diagnosis of 5 days (interquartile range = 0–46), among these cases (Figure 4). Thirty-two percent reached a diagnosis within the first month of presentation, with 16.3% more over the subsequent 11 months, and 49.8% did not have a documented final diagnosis in the EHR. The safety-net health system had a higher likelihood of reaching diagnosis than the academic medical center (odds ratio [OR] = 3.33, 95% confidence interval [CI] = 1.84–6.05). Otherwise, outcomes did not differ by clinician or patient characteristics, clinicians' level of diagnostic uncertainty,

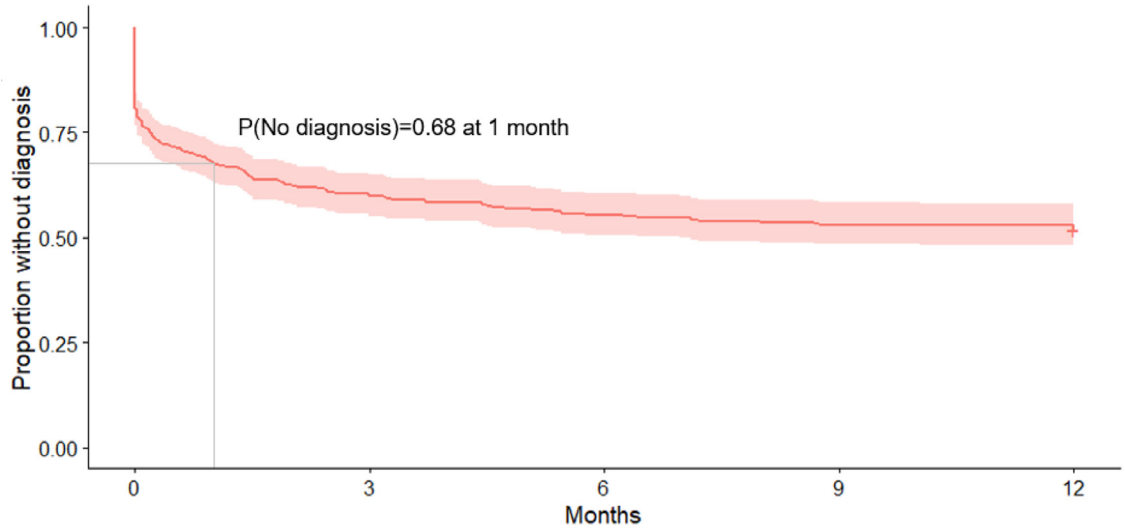


Figure 4: Shown in the graph is the Kaplan-Meier curve of time to diagnosis.

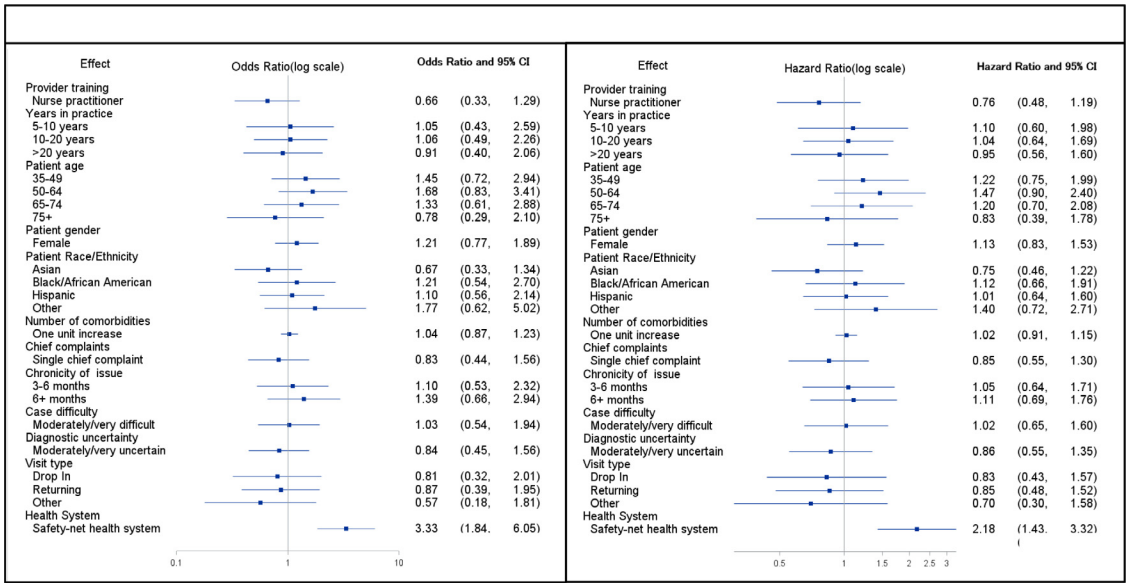


Figure 5: Shown here are forest plots of (A) predictors of the likelihood of having a final diagnosis within 12 months ($n = 410$), and (B) time to diagnosis among cases with a definitive diagnosis by 12 months ($n = 206$). CI, confidence interval.

chronicity of the medical issue, or type of visit (Figure 5). In our unadjusted bivariate model, medical complaints related to the circulatory (that is, cardiovascular) system were associated with a lower likelihood of having a definitive diagnosis within 12 months (OR = 0.34, 95% CI = 0.12–0.96) and longer time to diagnosis (hazard ratio = 0.45, 95% CI = 0.18–1.08) that did not reach statistical significance (Appendix Table 1). No other organ system was associated with likelihood or time to diagnosis (See Appendix Table 1 and Appendix Figures 1 and 2).

DISCUSSION

In a prospective cohort of 410 ambulatory care visits with a new or unresolved medical complaint followed over 12 months across two health systems, we found that only 50.2% of cases had a definitive diagnosis by 1 year, a frequency that highlights the challenges of medical diagnosis in primary care. There was heterogeneity between the two health systems, but we were struck by the pervasiveness of undiagnosed cases in both settings with more than one third of cases undiagnosed at 12 months. These unresolved diagnoses, which may represent diagnostic delays, were common across the board regardless of the clinician's level of experience or the patient's age, gender, or race. Clinicians' perception of diagnostic difficulty for an individual case was not associated with the likelihood of reaching a final diagnosis for that case. Finally, the undiagnosed cases spanned many organ systems and conditions. Our results suggest that interventions aimed at enhancing the diagno-

sis of one or a handful of conditions, as some experts have advocated,[13] may not address the range of diagnostic challenges in primary care.

Primary care encompasses a broad range of clinical concerns from common diseases to rare conditions to vague complaints that often make it difficult to pinpoint the underlying diagnosis. We suspect that even with optimal diagnostic processes, not all cases will reach a final diagnosis. However, researchers should undertake larger studies encompassing a wider range of care settings to determine whether our observed rates of unresolved diagnoses hold true. In our analysis, many of the undiagnosed cases were instances in which the provider documented the problem, performed a diagnostic investigation, and failed to pinpoint any abnormality. This may indicate that after ruling out actionable diagnoses, providers and patients simply moved on. Follow-up studies with direct inquiry of patients and providers would shed light on these cases and whether moving on without a diagnosis is associated with poor outcomes, particularly patient-reported outcomes.

The structure of primary care delivery—brief visits that generally occur months apart—presents a challenge to diagnostic excellence. Brief visits with frequent interruptions increase the cognitive challenge of making a correct and timely diagnosis, as has been widely reported in observational and simulation studies.[5,14,15] If a patient misses a scheduled follow-up appointment, it can easily extend the diagnostic time line beyond one year. Hence, factors at the level of the clinic or health system, such as practice delivery models, access to frequent appointments, and other operational health care processes could support diagnosis and contribute to high or poor performance in diagnostic excellence. For instance, the two health systems in this study differed in their likelihood of reaching a diagnosis. Potential explanations for this difference could include the employment of a team-based delivery model, whereby a system can facilitate more frequent visits and follow-up of unresolved conditions (such as abnormal laboratory results) led by nonphysician health care professionals.

To our knowledge, our study is the first prospective longitudinal study of diagnostic uncertainty in primary care, shedding light on diagnostic trajectories over time—a critical step for designing and testing innovations for improving diagnostic excellence in outpatient care. In our sample, the overwhelming majority of cases that were not diagnosed within a month of the first presentation remained undiagnosed at 12 months. This suggests that 1 month following the initial primary care visit may be an appropriate time to initiate intervention in undiagnosed cases. Furthermore, our study was conducted in two health care settings (a public delivery system and an academic medical practice), both serving a racially/ethnically diverse patient population, which may increase the generalizability of this study to other sites.

Given the pervasiveness of undiagnosed cases in our analysis, solutions will require a systematic approach rather than focusing on particular subpopulations or common medical complaints. This is consistent with prior work supporting and advocating employment of systems engineering to reduce diagnostic delays and improve patient safety.[16] For example, implementing an electronic checklist that includes unresolved medical complaints (for example, symptoms or lab abnormality) could empower patients and nonphysician members of the care team to follow up on the complaint until it is resolved—an example of the concept of "balanced work system."[17] The balanced work system model proposes that positive elements within the work environment compensate for challenges in the work system. In this example, a health information technology–based prompt and a nonphysician-led, patient-engaged workflow could serve to counter the challenge inherent in placing sole responsibility for diagnostic excellence and patient safety on the primary care provider. Promising interventions could include easy-to-use diagnostic clinical decision support tools embedded in the EHR. It is critical to conduct more prospective intervention studies of diagnosis in primary care to identify effective and feasible strategies to enhance the timeliness and accuracy of diagnosis.

Limitations

We note some limitations to consider in interpreting these findings. First, we enrolled a circumscribed number of providers, including internal medicine and family medicine physicians and nurse practitioners working in two delivery systems, and included cases based on specified a priori criteria. Although the two health systems encompass multiple settings and care for diverse patient populations, we acknowledge that the results should not be generalized across all primary care settings. Furthermore, although we adjusted for patient and provider characteristics, we could not assess clinic or system-level structures or processes that could explain heterogeneity at the level of the health system, as these factors are not captured in our EHR–derived data. Third, the primary care practitioners in this analysis were clinicians who participated in a trial of a diagnostic intervention, which also limits the generalizability of our findings. Nevertheless, we believe ours to be the largest prospective study of outpatient diagnosis to date. Furthermore, because these clinicians knew they were being "watched," a potential Hawthorne effect would bias our results toward a shorter time to diagnosis as compared to the general community of clinicians. We ascertained the final diagnosis via two-physician adjudication of the medical record. Although this is the gold-standard method for patient safety studies,[18–20] gaps in medical record documentation could have led to overestimation of unresolved diagnosis if clinicians arrived at a diagnosis and failed to document it. We attempted to address this limitation by including test results or empiric treatment as part of the adjudication data. Fur-

thermore, failed documentation itself could compromise patient safety and could be seen as a diagnostic mishap, if not an error. Our exploratory, unadjusted analysis suggested that undiagnosed cases could be more common in cardiac vs. noncardiac cases, but we could not establish whether there is an independent relationship between organ system and undiagnosed cases. This may warrant further exploration, but our findings indicate that undiagnosed cases were pervasive regardless of the organ system associated with the medical complaint. Last, we used an organ system designation to classify patients' chief complaints. Other methods of classification based on symptoms (for example, text processing and syndrome classification) could be explored in future studies to examine whether timeliness of diagnosis varies by types of symptoms.[21]

CONCLUSION

Taken together, our findings suggest that undiagnosed cases in primary care are significant and pervasive, and solutions to improving diagnosis in ambulatory care that focus on specific subpopulations or medical complaints may not address the range of diagnostic challenges in primary care. This problem warrants further observational study, including studies of EHR audit data and direct observation, as well as development and testing of system-based interventions in care delivery, to ensure timely resolution of medical complaints in primary care.

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REFERENCES

1. Ball JR, Balogh E. Improving diagnosis in health care: highlights of a report from the National Academies of Sciences, Engineering, and Medicine. Ann Intern Med. 2016 Jan 5;164:59–61.
2. Singh H, Meyer AND, Thomas EJ. The frequency of diagnostic errors in outpatient care: estimations from three large observational studies involving US adult populations. BMJ Qual Saf. 2014;23:727–731.
3. Kwan JL, Singh H. General internists in pursuit of diagnostic excellence in primary care: a #ProudtobeGIM thread that unites us all. J Gen Intern Med. 2018;33:395–396.
4. ALQahtani DA, et al. Does time pressure have a negative effect on diagnostic accuracy? Acad Med. 2016;91:710–716.
5. Coiera E. The science of interruption. BMJ Qual Saf. 2012;21:357–360.
6. Croskerry P, Sinclair D. Emergency medicine: a practice prone to error? CJEM. 2001;3:271–276.
7. Croskerry P. Achieving quality in clinical decision making: cognitive strategies and detection of bias. Acad Emerg Med. 2002;9:1184–1204.
8. Khoong EC, et al. Impact of digitally acquired peer diagnostic input on diagnostic confidence in outpatient cases: a pragmatic randomized trial. J Am Med Inform Assoc. 2021 Mar 1;28:632–637.
9. Fontil V, et al. Testing and improving the acceptability of a web-based platform for collective intelligence to improve diagnostic accuracy in primary care clinics. JAMIA Open. 2019 Feb 1;2:40–48.
10. Bhise V, et al. Electronic health record reviews to measure diagnostic uncertainty in primary care. J Eval Clin Pract. 2018;24:545–551.
11. ICD10Data.com. The Web's Free 2022 ICD-10-CM/PCS Medical Coding Reference. Accessed May 6, 2022. https://www.icd10data.com/.
12. Yurkovich M, et al. A systematic review identifies valid comorbidity indices derived from administrative health data. J Clin Epidemiol. 2015;68:3–14.
13. Newman-Toker DE, et al. Rate of diagnostic errors and serious misdiagnosis-related harms for major vascular events, infections, and cancers: toward a national incidence estimate using the "Big Three.". Diagnosis (Berl). 2021 May 14;8:67–84.
14. Weigl M, et al. The association of workflow interruptions and hospital doctors' workload: a prospective observational study. BMJ Qual Saf. 2012;21:399–407.
15. Hung GR, et al. Computer modeling of patient flow in a pediatric emergency department using discrete event simulation. Pediatr Emerg Care. 2007;23:5–10.
16. Carayon P. The Balance Theory and the work system model . . . twenty years later. Int J Hum Comput Interact. 2009;25:313–327.
17. Carayon P, et al. Human factors systems approach to healthcare quality and patient safety. Appl Ergon. 2014;45:14–25.
18. Raffel KE, et al. Prevalence and characterisation of diagnostic error among 7-day all-cause hospital medicine readmissions: a retrospective cohort study. BMJ Qual Saf. 2020;29:971–979.
19. Fink JC, et al. Patient-reported safety events in chronic kidney disease recorded with an interactive voice-inquiry dial-response system: monthly report analysis. J Med Internet Res. 2016 May 26;18:e125.
20. Zhao Y, et al. Development and validation of an algorithm to identify drug-induced anaphylaxis in the Beijing Pharmacovigilance Database. Int J Clin Pharm. 2018;40:862–869.
21. Lee SH, et al. Chief complaint classification with recurrent neural networks. J Biomed Inform. 2019;93:103158.