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Differential Diagnosis Documentation In Emergency Medicine

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Abstract:

Diagnosis is a central aspect of emergency medicine. Coming to the correct diagnosis impacts patient morbidity and mortality and also the healthcare expenditures. Medical decision making is driven by the path of figuring out the differential diagnosis. Once a decent Natural Language Processing (NLP) system is developed including general characterization of differential diagnose, associated with downstream testing, diagnostic error, etc., we could be able to automatically extract differential diagnoses within clinical notes, which would have a large impact on healthcare. The main purpose of our investigative study is the characterization of differential diagnosis documentation within emergency provider notes and the development of an annotated corpus which could be used for further downstream development of NLP applications. We conducted a retrospective analysis of emergency provider notes to identify, categorize, and extract information around differential diagnoses using manual annotation.We used a light annotation framework within the MATTER cycle, and extracted the information from our annotations based on a random sample of 1545 medical records. We describe the demographics information and note that only 18.1% of patients were actually given a differential diagnosis by the physicians. We examined factors including age groups, race and ethnicity groups, language preferred, acuity level and major complaints that could lead to differences in differential diagnosis rate among patients. Within the differential diagnosis groups, evidence support and probability terms are reported. We also examined cough, chest pain, shortness of breath, abdominal pain, back pain and falling, which are top six complaints. Still, we suffered from limitations including sample size, nature of the accuracy of annotations etc.

Acknowledgements

First and foremost, I would like to express my sincere gratitude to my advisors, Prof. Richard Andrew Taylor, and Dr. Katie(Xinxin) Zhu, who guided me through this project and played important roles in my academic path. You are more like my supportive friends, someone to work together, someone you could seek help from against my assumption of rigorous professors. I wouldn't find this interesting and meaningful topic as my master thesis without you. I am so grateful to meet you at Yale.

Besides my advisors, I would like to honor my beloved parents, though you are in China thousands of miles away, you are always my source of love and power. Hope your son would live up to your names.

Last, to my friends. My life is so colourful and bright because of you. The laughter and tears are so vivid and unforgettable. It's so lucky for me to meet you guys here. May the friendship forever last!

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Introduction

Diagnosis is a central aspect of emergency medicine(Cimino, Li, and Weng 2018). In few other specialties is a provider confronted with such a compressed time-frame with such an array of complaints spanning the breadth of medicine. The complaints could be deadly with an immediate need for treatment, like stroke or acute subarachnoid hemorrhage, or less time-sensitive like hypertension, or fatigue. Given the limited medical resources, emergency physicians have to make a quick decision with limited information and prioritize their work in a chaotic clinical environment. Having the right diagnosis allows physicians to take the appropriate next steps for treatment.

Coming to the correct diagnosis not only impacts patient morbidity and mortality, but also healthcare expenditures and a variety of other markers of quality care as well. For example, a recent report by the Institute of Medicine as part of the Quality Chasm Series entitled "Improving Diagnosis in Healthcare"(Care et al. 2015) highlighted the fact that diagnostic error is responsible for about 10% of patient deaths, and that "most people will experience a diagnostic error in their lifetime, sometimes with devastating consequences". The main reason for this diagnostic error is failure to consider certain diagnoses, which may share similar symptoms or even test results with the diagnosis(Cassou-Mounat et al. 2020).

Based on the reasons above, differential diagnosis is a crucial step for medical decision making. By listening to the patients' chief complaint, emergency medicine physicians work through potential diagnoses tep by step, utilizing the physical exam and lab tests to narrow down the reasons and ultimately arrive at the final diagnosis in the limited time. The information leading to a diagnosis and the evaluation for differential diagnosis could consist of many pieces of fragmented information. For example, one patient with difficulty in breathing comes to the emergency medicine, after getting his chief complaints, physicians need to figure out what's the reasons causing this problem. Swallowing something could be one reason, especially for the young kids(Reynolds, Grider, and Bell 2017), adults sometimes, thus physicians should ask it during the interview, and check during the physical exam. And during the physical exam, physicians may listen to the murmur on chest, to see the heartbeat sound and breath sound. Differences could be observed if pathological changes occur(Wilkins 2009). As severe pneumonia could lead to difficulty in breathing(Wilkins 2009; Fernando et al. 2020), physicians also have to order chest X-ray to see. Besides, by asking the medical history, physicians could get useful information as well. If the patients have had any cardiovascular diseases or like hypertension, they may suffer from chronic heart failure as well, which may cause breath difficulty as the ejection ability gradually goes down and blood congested in the lung(Francis 2001; Bussmann 1986).

Medical decision making is driven by the path of figuring out the differential diagnosis by exams, tests. And the ability to explore differential diagnosis is also a key component in medical education. This deduction and analysis ability mentioned above is what medical students are learning everyday at medical school through the case discussion(Croskerry 2017). We give credit to the hard work of medical students and physicians generations by generations, but we have to admit that the way of getting a diagnosis has not changed for a long time. While the convenience of the internet and data has brought us into a new era, how to leverage it into the medical region is our consideration.

In the classic hypothetico-deductive clinical reasoning model, formulation of a different diagnosis is the key aspect of the diagnostic process, guiding all subsequent clinical inquiry(Cimino, Li, and Weng 2018). While providers frequently document this reasoning process within clinical notes, often in the form of lists with qualifiers to note different levels of clinical suspicion about a particular diagnosis, very little is known about the level of documentation, subsequent care decisions based on these differential diagnoses lists, or the ultimate diagnosis made for any particular visit mainly because natural language processing, search, and retrieval are challenging and no gold standard corpus exists for training. As such, there is currently no automated system for extracting differential diagnoses within clinical notes.

Once a decent Natural Language Processing (NLP) system is developed including general characterization of differential diagnose, associated with downstream testing, diagnostic error, etc., we could automatically extract differential diagnoses within clinical notes, which would have a large impact on healthcare.

Research Design

- **Research goal**

The main purpose of our investigative study is the characterization of differential diagnosis documentation within emergency provider notes and the development of an annotated corpus which could be used for further downstream development of NLP applications. We extract the information from our annotations based on a random sample of 1545 medical records. We use CLAMP, a clinical Natural Language Processing (NLP) software that enables recognition and automatic encoding of clinical information in narrative patient reports, to note the full range of differential diagnosis, we combine this with demographic information of the patients including their age groups, sex, race, ethnicity, preferred languages, acuity level, and financial class(insurance), etc. Also, we determine the differential diagnosis and the features related to it, including major complaints, probability, evidence terms. By conducting multivariable regression analysis, we determine the factors leading to a significant difference in differential diagnosis ratio. Once we set up the standard corpus of emergency department providers' notes, we hope to further develop and validate a natural language processing system to automatically identify and classify differential diagnoses within emergency department provider notes in the future.

- **Research method**

It's a retrospective analysis of emergency provider notes to identify, categorize, and extract information around differential diagnoses using manual annotation, EHR data extraction, and statistical methods for further data characterization..

Informed consent was waived by the IRB. All patients who previously indicated the desire to opt out of EHR-based research were excluded.

- **Study Setting and Population**

The training and validation cohort was derived from patients presenting to 1 of 4 EDs over a 4-year time period (March 2015 through March 2019). All EDs are part of a single health care system. One is an urban, academic, level 1 trauma center with 85,000 annual visits; the second ED is an urban level 2 trauma center with 70,000 annual visits, the third ED is a community-based, urban, and an auxiliary training site for emergency medicine residents with an annual census of approximately 77,000 annual visits, and the fourth ED is a suburban free-standing community-based center with approximately 30,000 annual visits.

- **Annotation and analysis Methods**

We used annotation as a means to label differential diagnoses within encounters and identify important text features of these differential diagnoses including language around probability or clinical certainty. We used a light annotation framework within the MATTER cycle.

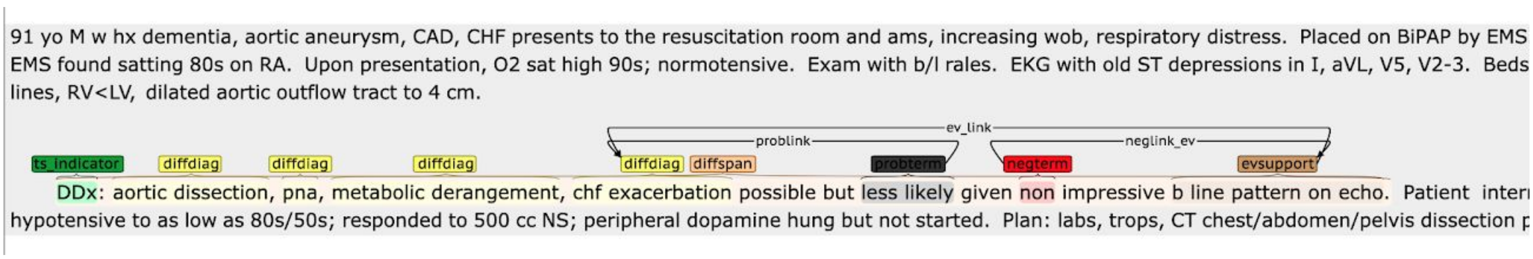
For annotation tasks and incorporation of annotations into machine learning categorization we adhered to the MATTER cycle. The model can be described as a set of three components M = (T,R,I) where M is the model, T is the set of terms being used, R is the relations between terms, and I is the interpretation of the terms and relations. Model and annotation development will go through an iterative process on a sample of documents, referred to as MAMA (model annotate model annotate), where problems are worked out and the final versions are determined. The training, testing, and evaluation steps are where the machine learning algorithm is taught to recognize features, tested and evaluated. Revise is the final step at which the entire process is reviewed.

We adhered to a light annotation framework to optimize resources on the specific task of differential diagnosis identification and categorization(Finlayson and Erjavec 2017). The concept of light annotation task (for domain specific annotation) is a linguistically under-specified, task- and domain-specific model that potentially overlaps with a full and more resource intensive annotation task. A light annotation task is used to quickly capture domain specific knowledge in a corpus as it relates to a research question but does not require trained investigators to perform intensive annotation. The end result is a dataset that represents complex information but that is itself not complex and that is in a format that will not conflict with any tags or labels that might be applied in future tasks.

We developed a light annotation schema using a multi-staged approach. First, we leverage concepts from prior literature and record general statements that declare in broad terms the annotation goals. As an example, the annotation goal could be "Identify all differential diagnoses?" Next, we used a multi-stage iterative coding approach to sample sets of texts to enumerate specific variables and relationships to be considered when annotating. Iterative coding has been applied to the biomedical domain for many studies including discovery of clinical conditions in emergency medicine notes. The iterative coding approach involves reading and re-reading text to develop a schema/codebook that can be used for light annotation(Finlayson and Erjavec 2017; Chapman and Dowling 2006).

We adhered to the method of text-bound annotation (i.e., we will associate all annotation with actual expression in text) to ensure a higher likelihood of inter-annotator agreement. We anticipate annotation tags to cover entities/relationships pertinent to differential diagnosis, modifier tags that communicate clinical uncertainty, link tags, and non-consuming tags.

Within our annotation tags here, we have tags “ts_indicator”, “diffdiag”, “probterm”,“evsupport”, “negterm”, “diffspan”:The “ts_indicator” means the indicator for a differential diagnosis within the physician notes, words like “ddx”, “differential diagnosis”, “other possible considerations”,etc. which indicate the following information might be differential diagnosis. The “diffdiag” means the differential diagnosis mentioned, listed after the indicators. The “probterm” tag is the probability description for each differential diagnosis, like “low suspicion”, “probable”, “likely”, so as to sort the possibility for different differential diagnosis. The “evsupport” means the evidence supporting or not supporting the differential diagnosis, like lab tests or symptoms. The “negterm” is like “not”, “no”, are terms before evendice or diagnosis. The “diffspan” is the whole paragraph related to the differential diagnosis part. This is our taggings and logic under our selections. The figure below is a representative illustration of our annotations.



For the annotation task we selected the ED provider notes. Within these texts we adhered to span level, as opposed to document level, phenotype classification.

Annotators were trained physicians. We measured the schema’s completeness, the annotator's ability to apply the schema with high agreement through adjudication procedures.

Regression analysis

Standard descriptive analyses were performed on data stratified by differential diagnosis documentation result. To examine the association between patient and provider features with differential diagnosis documentation, logistic regression was performed. The overall peformance of the model was assessed with the Hosmer-Lemeshow statistic. Multi-collinearity was checked by variance inflation factor (VIF) and influential variables and additional outliers by Cook’s distance. All variables had a VIF \textless 3 and there were no significant outliers. Results from the logistic regression are presented as an odds ratio with 95\% Confidence Intervals (CI).

Results and discussion

a. Summary of findings

To analyze the 1545 records, we sorted the patients into two groups, differential diagnosis group and no differential diagnosis group. The table below describes the demographics and other information associated with the patients, including their preferred languages, the acuity level of the case, and their financial class(insurance). Among the information here, we could figure that there are only 18.1% of patients who were actually given a differential diagnosis by physicians. Although not all cases necessarily need a differential diagnosis given their symptoms, physical exams and lab tests results, the percentage is still below our expectation, as we generally explore other possible explanations for the diseases before we make the medical decisions. The relatively low differential diagnosis rate could be partially justified given the limited timeframe and urgency in emergency medicine,

As to the age group, by comparing the rates of differential diagnosis here, we figured that the age group 0-18 has a higher proportion of getting differential diagnoses, which infers that pediatric diseases are more likely to be given a differential diagnosis compared with other diseases. But this could be possibly confounded by the relatively weak or ambiguous self-description of major complaints given the young age of this group.

		Grouped by differential Diagnosis	
		No differential Diagnosis Group	Differential diagnosis group
Patients		1266	279
Age		42.0 [23.0,59.0]	27.0 [10.0,54.0]
Age Groups	Age 0-18	224 (17.7)	105 (37.6)
	Age 18-44	466 (36.8)	81 (29.0)
	Age 45-64	343 (27.1)	48 (17.2)
	Age 65+	233 (18.4)	45 (16.1)
Sex	Female	671 (53.0)	128 (45.9)
	Male	595 (47.0)	151 (54.1)
Race	Black or African American	315 (24.9)	77 (27.6)
	Other	274 (21.6)	78 (28.0)
	White or Caucasian	677 (53.5)	124 (44.4)
Ethnicity	Hispanic or Latino	281 (22.2)	80 (28.7)
	Non-Hispanic	969 (76.5)	197 (70.6)
	Other	16 (1.3)	2 (0.7)
PreferredLanguage	English	1119 (88.4)	241 (86.4)
	Other	28 (2.2)	13 (4.7)

	Spanish	119 (9.4)	25 (9.0)
AcuityLevel	*Unspecified	10 (0.8)	
	Emergent	240 (19.0)	78 (28.0)
	Immediate	3 (0.2)	3 (1.1)
	Less Urgent	361 (28.5)	57 (20.4)
	Non-Urgent	83 (6.6)	17 (6.1)
	Urgent	569 (44.9)	124 (44.4)
FinancialClass	BCBS	152 (12.0)	32 (11.5)
	Commercial	41 (3.2)	6 (2.2)
	Managed Care	188 (14.8)	44 (15.8)
	Medicaid	468 (37.0)	126 (45.2)
	Medicaid Managed Care	16 (1.3)	1 (0.4)
	Medicare	240 (19.0)	37 (13.3)
	Medicare Managed Care	56 (4.4)	13 (4.7)
	Other	7 (0.6)	4 (1.4)
	Self-pay	83 (6.6)	14 (5.0)
	Worker's Comp	15 (1.2)	2 (0.7)

We further conducted a multivariate regression analysis including the factors above to analyze the potential factors leading to a difference in differential diagnosis rate. As shown in the table below, the age group under 18 has a higher Odds Ratio compared with the other age groups. We could also find a higher proportion of pediatric diseases in file.

As to race and ethnicity groups, we could see that non-hispanic and white or Caucasian groups are around the borderline significance. Given the fact that our sample size is 1545 patients, and only 18% have a differential diagnosis, the results could possibly be more significant if we enroll more patients in the future. And this suggests a higher differential diagnosis rate among the hispanic group population.

Another finding is the other language speaking group, compared with the English speaking group, has a higher odds ratio. To find out the potential reasons leading to this difference, we did a literature review but found little research related to this topic. One assumption could be the use of translators inevitably increased the treatment time for other language speakers. And this longer and more detailed communication with physicians contributes to the higher ratio of differential diagnosis.

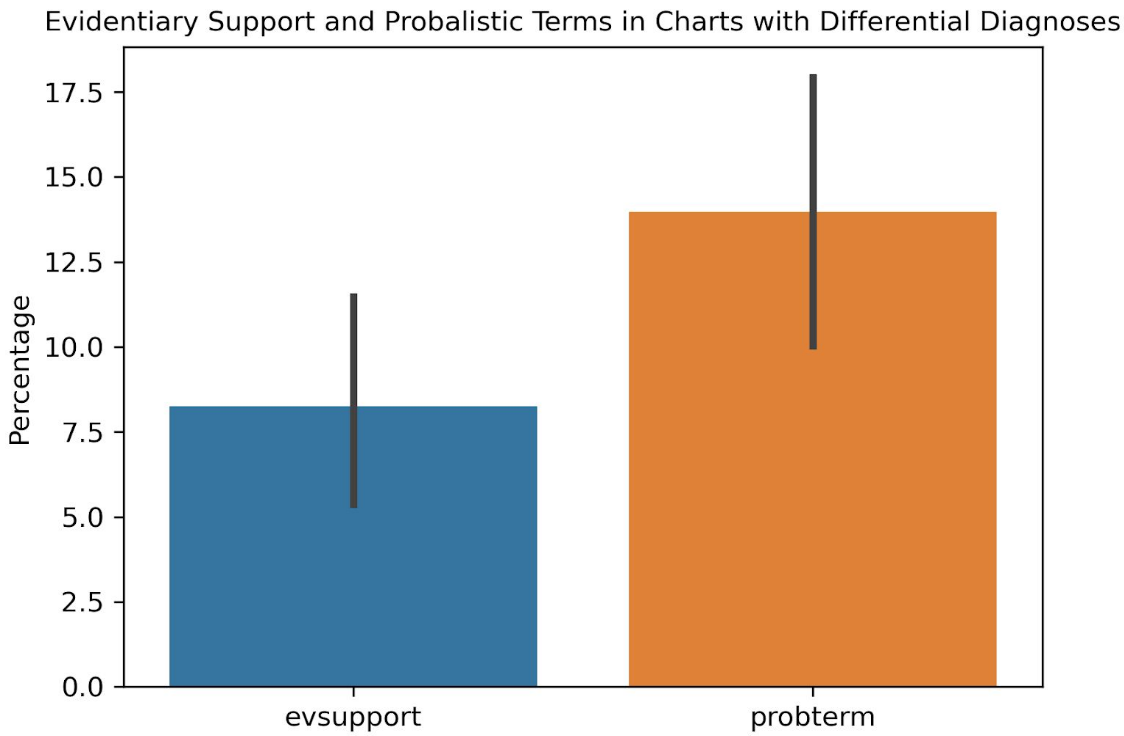
Among all symptoms and major complaints of the patients, we select six representative and common ones to analyze, they are back pain, chest pain, cough, fall, shortness of breath and others respectively. Among them, chest pain has the highest proportion for the differential diagnosis group. From what we know from previous studies(Moriber 2017) and the medical decision making process(Stepinska et al. 2020), there are many diseases that could lead to chest pain. Besides, some diseases regarding chest pain could be deadly, for instance, acute coronary disease, they are red signs and get more attention from physicians as well.

As to acuity, we figured that the lower acuity group has a relatively high rate to get more differential diagnosis. Given its non-urgent conditions, physicians could have more time for thorough physical exams, medical history taking, and wait until all lab results come back to give a more informative decision. This could explain the higher rate here.

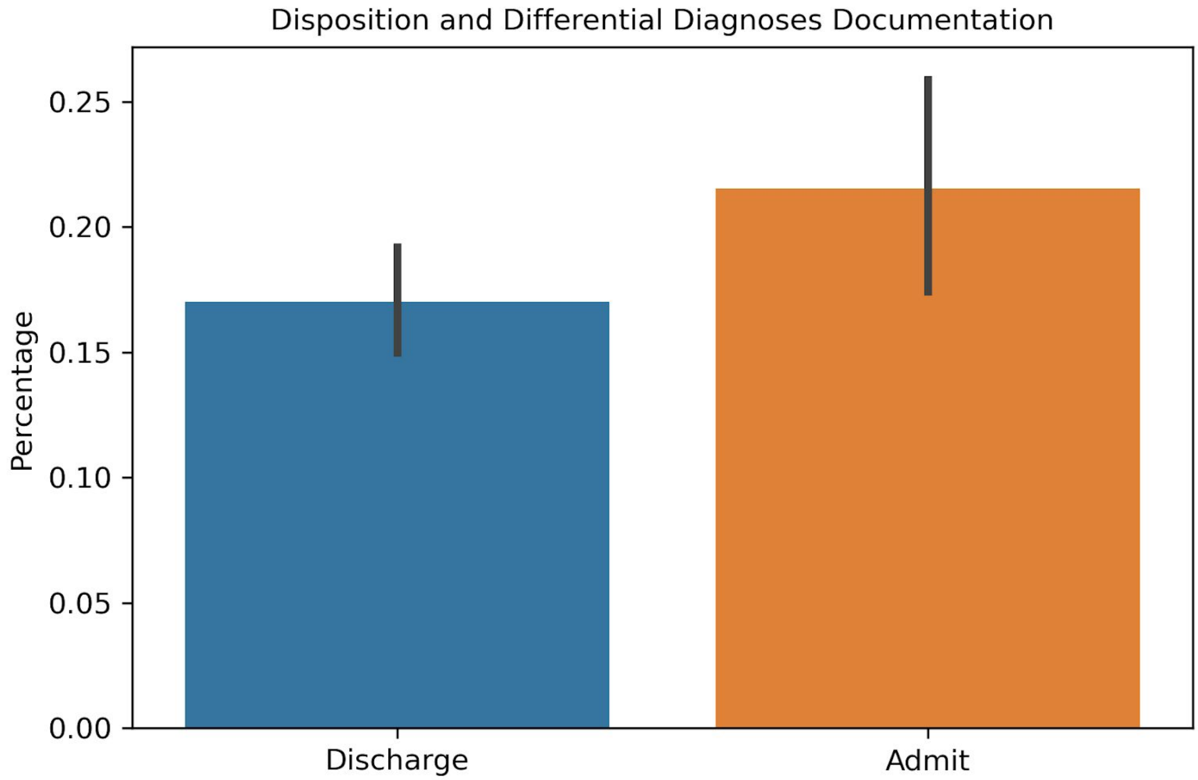
Categories	5%	95%	Odds Ratio
Intercept	0.39	2.01	0.89
Age(years)			
0-18	Ref.	Ref.	Ref.
18-44	0.24	0.48	0.34
45-64	0.17	0.40	0.26
65+	0.23	0.85	0.44
Race			
Black or African American	Ref.	Ref.	Ref.
Other	0.50	1.41	0.84
White or Caucasian	0.49	1.00	0.70
Ethnicity			
Hispanic or Latino	Ref.	Ref.	Ref.
Non-Hispanic	0.39	1.01	0.63
Other	0.09	2.03	0.43
FinancialClass(Insurance)			
BCBS	Ref.	Ref.	Ref.
Commercial	0.34	2.33	0.89
Managed Care	0.68	1.95	1.15
Medicaid	0.61	1.53	0.96
Medicaid Managed Care	0.02	1.22	0.15
Medicare	0.40	1.51	0.77

Medicare Managed Care	0.48	2.66	1.12
Other	0.65	9.68	2.50
Self-pay	0.42	1.80	0.87
Worker's Comp	0.23	5.36	1.12
Acuity Level			
Higher acuity	Ref.	Ref.	Ref.
lower acuity	0.37	0.71	0.51
Major Complaint			
Abdominal pain	Ref.	Ref.	Ref.
BACK PAIN	0.47	3.20	1.23
CHEST PAIN	1.03	4.24	2.09
COUGH	0.80	4.03	1.80
FALL	0.20	1.68	0.58
OTHER	0.75	2.13	1.27
SHORTNESS OF BREATH	0.59	3.40	1.42
Preferred Language			
English	Ref.	Ref.	Ref.
Other	1.09	4.97	2.33
Spanish	0.36	1.10	0.63

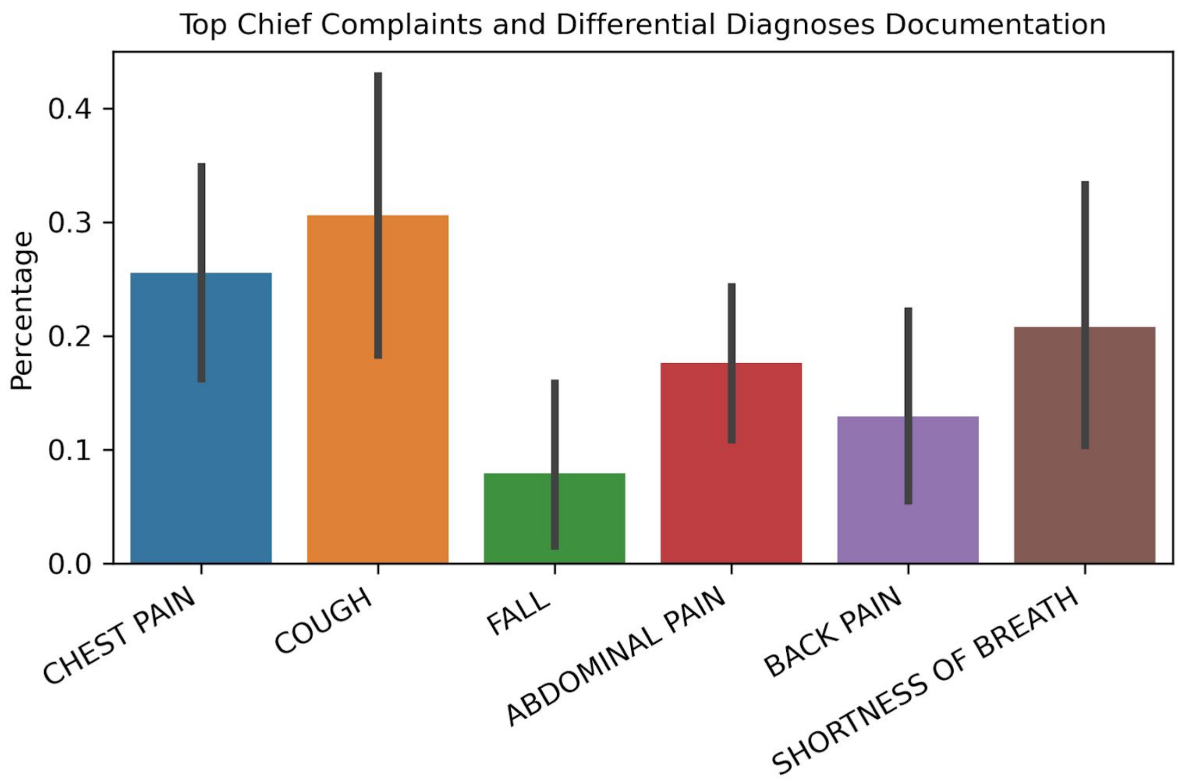
Within the differential diagnosis groups, we did an analysis to explore some features as well and the followings are our further findings. Among all the patients with a differential diagnosis in the records, only around 8% have specific evidence mentioned supporting them. Possible explanations could be the differential diagnosis share similar findings with the diagnosis, which were included through the whole medical records through exams, symptoms and lab test, thus they are not listed out under differential diagnosis span. As to the probability terms, it’s slightly higher around 14%. The possibility terms could be important in differential diagnosis, as this could influence the following treatment and medical management plan, prioritizing the most possible differential diagnosis first. With the project going on, we will further divide and sort the possibility that probability terms referred to.



We then compared the disposition and its relationship with differential diagnosis. We could tell from the graph below that the admitted rate is slightly higher, but to confirm its significance we still need to enlarge our sample size.



We could see cough, chest pain, shortness of breath, abdominal pain, back pain and falling are top six complaints. Among them, falling has the lowest rate for differential diagnosis, which may due to its nature of traumatic disease, which is more easily to have a clear diagnosis. And as our next step is to develop the "gold corpus" for emergency physician notes annotation, these chief complaints could be a great starting point in the future.



b. Limitations of findings and other limitations of the study

One limitation of our findings here lies in the sample size. Within 1545 records annotated and analyzed, only 279 of them have differential diagnosis. To confirm the significance of the factors related to differential diagnosis, to develop gold corpus for further investigation, we need more annotated records in the future.

As to annotation itself, there are some spaces hard to define in physician notes whether or not they are referring to a differential diagnosis. As a differential diagnosis to diseases, it should be a disease which is possible and related to the patients based on the physicians findings. While in real practice, we figured that though some physicians would list a couple diseases saying they are differential diagnoses. But when compared with the diagnosis, they would list a couple reasons arguing why differential diagnoses are not possible to be a final diagnosis instead of listing reasons why they are plausible alternative explanations. This is in conflict with the nature of differential diagnosis itself which leads to the ambiguity and confusions. As we suggested previously, adding more proper and ranked probability terms describing the differential diagnosis could contribute to improving this situation.

Some other diseases, like mind issues, could have many differential diagnoses as well. But within the medical records we annotated, they seldom got any space in differential diagnoses. One possible reason could be psychiatry is a relatively distinct specialty, and physicians would generally refer these patients to psychiatrists and thus no differential diagnosis noted from their side.

Competency match

This research matches the MPH and CDE Competency requirement in the following:“Evidence-based Approaches to Public Health”, “Public Health & Health Care Systems”, “communication” and “overall thinking”.

For “Evidence-based Approaches to Public Health”, we selected 1545 emergency medicine medical records, come up with tagging logic and contents based on a variety of literature reviews, and use the CLAMP as our tagging environment to annotate the notes. We further discussed our results as described above.

For the “Public Health & Health Care Systems”, given the importance of diagnosis and differential diagnosis in emergency medicine, we try to come up with a gold standard corpus based on 1545 annotated emergency medicine medical records, and set up a decent Natural Language Processing (NLP) system in the long run, which includes general characterization of differential diagnose, associated with downstream testing, diagnostic error, etc. This could potentially change the differential diagnosis and medical decision making in the future, with a shorter time frame, lower expenditure and a more efficient healthcare system as well. Like the pandemic days, if enough records are gathered for Cov-19 patients, NLP would assist doctors to give differential diagnosis besides Cov-19 in a short time frame, which could help to lower the working load given this limited medical resources.

For overall thinking and communication competency, we try to leverage the clinical NLP software CLAMP to recognize and encode the clinical information in narrative patient reports, where we applied the advanced computer science tech into the field of medicine. With its help, we managed to annotate the narrative medical records and determine the differential diagnosis and the features related to it, including major complaints, probability, evidence terms. We also draw the demographic information and determine the factors leading a difference in differential diagnosis via multivariable regression analysis. With the features we determined and annotated records, we could further develop a gold corpus for ER annotations in the future, and leverage machine learning to train and learn to achieve autonomous differential diagnosis detection in the long term. This process has involved and will further include experts with diverse backgrounds in medicine, public health, computer science, which offers me a great opportunity to explore the field outside epidemiology, and learn how to communicate with people in a totally different background, knowledge and skill sets. This process could be challenging, inspiring and worth learning.

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