Cultivating informatics capacity for multimorbidity: A learning health systems use case

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Abstract

Background: The aim of this study was to characterize patterns of multimorbidity across patients and identify opportunities to strengthen the informatics capacity of learning health systems that are used to characterize multimorbidity across patients.

Methods: Electronic health record (EHR) data on 225,710 multimorbidity patients were extracted from the Arkansas Clinical Data Repository as a use case. Hierarchical cluster analysis identified the most frequently occurring combinations of chronic conditions within the learning health system's captured data.

Results: Results revealed multimorbidity was highest among patients ages 60 to 74, Caucasians, females, and Medicare payors. The largest numbers of chronic conditions occurred in the smallest numbers of patients (i.e., 70,262 (31%) patients with two conditions, two (<1%) patients with 22 chronic conditions). The results revealed urgent needs to improve EHR systems and processes that collect and manage multimorbidity data (e.g., creating new, multimorbidity-centric data elements in EHR systems, detailed longitudinal tracking of compounding disease diagnoses).

Conclusions: Without additional capacity to collect and aggregate large-scale data, multimorbidity patients cannot benefit from the recent advancements in informatics (i.e., clinical data registries, emerging data standards) that are abundantly working to improve the outcomes of patients with single chronic conditions. Additionally, robust socio-technical system studies of clinical workflows are needed to assess the feasibility of integrating the collection of risk factor data elements (i.e., psycho-social, cultural, ethnic, and socioeconomic attributes of populations) into primary care encounters. These approaches to advancing learning health systems for multimorbidity could substantially reduce the constraints of current technologies, data, and data-capturing processes.

Keywords

multimorbidity, electronic health record, informatics, learning health system, patterns

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Introduction

Individuals living with two or more chronic conditions (i.e., multimorbidity) face substantial health challenges that require ongoing medical attention and limit activities of daily living.^{1–9} Multimorbidity is associated with higher mortality rates, worsened functional status, and diminished quality of life when compared to those who have one or no chronic conditions.^{2–4} Nationally, 81% of Americans ages 65 and older have multimorbidity.^{4,5} However, multimorbidity is expanding beyond its traditional associations with elderly and aging populations, with 50% of Americans ages 45 to 65 having multiple chronic conditions.^{5–13}

Arkansas has been ranked as having the second-highest multimorbidity prevalence of all 50 states in adults ages 18-45,⁵ reflecting the substantial burden of multimorbidity on healthcare systems. Yet, patterns of how multimorbidity is occurring among populations remain underexamined at national and more localized levels, restricting what is known about multimorbidity to focus on estimating the dyads and triads of the most frequently combinations of chronic conditions in Arkansas. Consequently, attempts at elucidating how multimorbidity is occurring have been heavily constrained by the lack of integrated technologies and opportunities for data aggregation that exists within the domain of biomedical informatics.¹³⁻²⁵ Examining the capacities of the learning health systems (LHS) and processes in which multimorbidity data are collected and managed has not been prioritized,¹⁴⁻³⁰ leaving much of what is known about multimorbidity to focus on simply revealing patterns of chronic conditions among elderly patients (i.e., ages ≥ 65). Therefore, the aim of this study was to 1) characterize patterns of multimorbidity across patients, more broadly, among all demographic groups (i.e., age, gender, race, and ethnicity) and 2) concurrently, identify opportunities to strengthen the informatics capacity (i.e., technologies, data, and processes) of a learning health system, using the Arkansas Clinical Data Repository as a use case. More specifically, the study was guided by the following research questions: 1) what are the patterns of multimorbidity across patients, stratified by age, gender, race, and ethnicity and 2) what opportunities exist to strengthen the informatics capacity of learning health systems that are used to characterize patterns of multimorbidity across patients?

The characterization of multimorbidity in learning health systems

Learning health systems are data-driven, healthcare delivery processes of continuous quality improvement, providing patients with higher quality, safer, and more effective care by utilizing informatics and data science to translate research into evidence-based practice.^{31,32} However,

opportunities to improve multimorbidity patient outcomes are widely constrained by the current informatics infrastructure that is used to characterize the outcomes of patients with multimorbidity.^{2,4,6,31–35} To date, these informatics constraints have included the subjectivity (i.e., recall bias) of analyzing self-reported data gathered through national databases (i.e., National Health Interview Survey) and the focus on specific sets of chronic conditions versus all combinations that could potentially encompass multimorbidity (i.e., Behavioral Risk Factor Surveillance System *Surveys*).^{2,6} Additionally, the exclusion of institutionalized adults (long-term care settings, correctional facilities, etc.) has been a significant constraint of using national databases to examine multimorbidity, leading to the underreporting of chronic conditions.⁴ However, the informatics capacity within learning health systems can be improved to address the siloed and fragmented clinical data which constrains the sharing of knowledge that supports improvements in the care outcomes of patients with multimorbidity.

Methods

Ethics declaration statement

The study protocol (#262593) was reviewed and approved by the Institutional Review Board at the University of Arkansas for Medical Sciences (UAMS).

Study design and participants

As a retrospective, cross-sectional study, electronic medical record (EMR) data were extracted from the Arkansas Clinical Data Repository (AR-CDR) in Little Rock, AR. The AR-CDR's data warehouse contains longitudinal data, regularly imported from the UAMS EHR, which collects data from encounters with patients throughout Arkansas. The AR-CDR is a comprehensive resource containing patient information (i.e., demographics, diagnoses, charges, and laboratory data).³³ Within the AR-CDR, data are deidentified, cleaned, transformed, and stored. The AR-CDR, supported by a Clinical and Translational Science Award, has facilitated advances in medical research through the effective recruitment of research subjects and supports secondary use of clinical data.³³ The AR-CDR is the core of the University of Arkansas for Medical Sciences' Learning Health System (UAMS LHS), utilizing informatics, data, and evidence-based practice to improve care quality, safety, and efficiency.^{31–35}

Inclusion criteria used to identify patient records in this study were 1) a diagnosis of two or more chronic conditions through at least one primary care encounter between 1 January 2014, and 1 July 2021, and 2) an age of 18 years or older. Patients who were under the age of 18 at any time during the study period were excluded. Race, ethnicity,

gender, socioeconomic, and insurance status were not used as inclusion criteria.

Multimorbidity and chronic condition selection

Chronic conditions were identified using the International Classification of Diseases Rv.10 (ICD-10) codes and limited to the Centers for Medicare and Medicaid's formally recognized list of chronic conditions.¹ To obtain a comprehensive view of all potential patterns occurring within the multimorbidity population. 29 ICD-10 codes identified the following conditions: AIDS; alcohol abuse; anemia deficiency; blood loss anemia; cardiac arrhythmias; chronic pulmonary disease; coagulopathy; congestive heart failure; depression; diabetes, complicated; diabetes, uncomplicated; drug abuse; fluid and electrolyte disorders; hypertension, complicated; hypothyroidism; liver disease; lymphoma; metastatic cancer; neurological disorders; obesity; paralysis; peripheral vascular disorders; peptic ulcer disease; psychoses; pulmonary circulation disorders; renal failure; rheumatoid arthritis and collagen vascular diseases; solid tumor without metastasis; and valvular disease.

Data collection and analysis

Discrete variables of interest were gender, race, ethnicity, insurance provider type, and chronic condition diagnoses (i.e., ICD-10 codes). Age intervals were constructed based on gaps and recommendations for better categorizing multimorbidity across patients.^{4–7,14–18} Age (i.e., 18–105), the only continuous variable, was examined by intervals (i.e., 18-30, 31-44, 45-59, 60-74, 75-88, and 89-105). Upon extraction of data from the AR-CDR, all variables were cleaned (i.e., removing duplicates, missing data) using Google Open Refine 2.0. Descriptive statistics (means, medians, modes, and frequencies) were calculated using IBM SPSS V.27 to characterize demographic variables. To provide a more robust identification of multimorbidity characteristics, descriptive statistics were stratified by three groups (i.e., patients with two chronic conditions, patients with three chronic conditions, and patients with four or more chronic conditions). Google Open Refine 2.0 was also used to perform hierarchical cluster analysis, identifying the top five most frequently occurring combinations of chronic conditions: stratified by age, race, ethnicity, and insurance payor.

Results

Data extraction identified an overall study population of 225,710 patients who met the study's inclusion criteria. Figure 1 reflects the number of chronic conditions of multimorbidity patients in the total study sample. The patterns of chronic conditions within each patient generally

occurred in smaller numbers (circled). For example, there were 70,262 (31%) patients with multimorbidity in the population that had only two chronic conditions as opposed to two (<1%) patients with 22 chronic conditions.

When further stratified by the number of total chronic conditions, there were 152,710 (67.7%) multimorbidity patients with three chronic conditions and 105,659 (46.8%) multimorbidity patients with four or more chronic conditions. Table 1 provides study demographics, stratified by the total number of chronic conditions. Multimorbidity patients with two chronic conditions had a mean age of 56.87 and a SD of 18.13, as compared to a mean age of 58.87 and an SD of 17.48 for multimorbidity patients with three chronic conditions. Multimorbidity patients with four or more chronic conditions had a mean age of 60.44 and an SD of 16.81. Median ages for each group were 59, 61, and 62 for patients with two, three, or four or more chronic conditions, respectively. In terms of age, patients ages 60 to 74 had the highest percentage of multiple chronic conditions with 30%, 32%, and 34% having two, three, or four or more chronic conditions, respectively. Although patients ages 89 to 105 had the lowest percentage of multiple chronic conditions with 3%, 4%, and 4% of patients with two, three, or four or more chronic conditions, respectively.

Table 1 reflects several patterns of multimorbidity across patients. First, the total number of chronic conditions increased among patients over time between ages 18 to 74, but were smaller in number (7396) among those that were 89 years or older. Second, Caucasian Americans were the largest racial group within the total study population with multimorbidity accounting for 62%, 63%, and 63% of patients that had two, three, or four or more chronic conditions, respectively. African Americans, as the second largest group with multimorbidity, had 28%, 29%, and 30% of patients with two, three, and four or more chronic conditions, respectively. Third, female patients accounted for 60%, and males accounted for 40% of all patients with multimorbidity. Finally, within insurance providers, Medicare was the primary payor for 36%, 41%, and 46% of patients with multimorbidity that had two, three, or four or more chronic conditions, respectively.

Hierarchical cluster analysis and multimorbidity combinations

Hierarchical cluster analysis identified 53,288 combinations of chronic conditions that existed within the overall study population of 225,710 patients with multimorbidity who had two chronic conditions. Tables 2–4 present the top five most frequently occurring combinations of chronic conditions that were identified, stratified by age and gender (Table 2), age and race (Table 3), and age and ethnicity (Table 4).



Figure 1. Number of patients with multimorbidity by the number of chronic conditions.

Among patients of all ages with two chronic conditions (Table 2), the most frequently occurring combination of chronic conditions was diabetes with hypertension in males (3267 [4%]) and hypertension with obesity in females (3788 [3%]). Among patients ages 18 to 30, the most frequently occurring combination of chronic conditions was depression with psychoses in both males (678 [11%]) and females (1182 [8%]). Among patients ages 31 to 44, the most frequently occurring combination of chronic conditions was hypertension with obesity in both males (502 [4%]) and females (1182 [4%]). Among patients ages 45 to 59, the most frequently occurring combination of chronic conditions was uncomplicated diabetes with hypertension in males (999 [4%]) and hypertension with obesity in females (1104 [4%]). Diabetes with hypertension was the most frequently occurring chronic condition combination in males and females ages 60 to 74 (1400 [5%] males and 1342 [4%] females) and males and females ages 75 to 88 (579 [4%] males and 615 [3%] females). Among patients ages 89 to 105, the most frequently occurring combination of chronic conditions was hypertension with neurological disorders in both males (64 [4%]) and females (144 [3%]).

Among all ages of patients with multimorbidity, uncomplicated diabetes with hypertension was the most frequently occurring combination of chronic conditions among Caucasian Americans (3615 [3%]), Asian Americans (56 [4%]), and American Indian and Alaskan Natives (24 [4%]) (Table 3). Hypertension with obesity was the most frequently occurring combination of chronic conditions among African American patients (2430 [4%]) of all ages. Among all ages of Native Hawaiian and other Pacific Islanders, diabetes (complicated and uncomplicated) with hypertension was the most frequently occurring chronic condition (56 [9%]).

Among patients with multimorbidity ages 18 to 30, depression with psychoses was the most frequently occurring combination of chronic conditions among Caucasian Americans (1124 [11%]), African Americans (475 [6%]), Asian Americans (17 [15%]), and American Indian and Alaskan Natives (4 [5%]) (Table 3). Anemia deficiency with blood loss anemia was the most frequently occurring combination of chronic conditions among Native Hawaiian and other Pacific Islanders in this age group (4 [11%]).

Among patients with multimorbidity ages 31 to 44, depression with psychoses was the most frequently occurring combination of chronic conditions among Caucasian Americans (822 [4%]) (Table 3). Hypertension with obesity was the most frequently occurring combination of chronic conditions among African Americans (823 [6%]) ages 31 to 44. Anemia deficiency with blood loss anemia was the most frequently occurring combination of chronic conditions among Asian Americans (20 [6%]) and American Indian and Alaskan Natives (8 [5%]). Uncomplicated diabetes combined with complicated diabetes was the most frequently occurring combination of chronic conditions among Native Hawaiian and other Pacific Islanders in this age group (19 [15%]).

Among patients with multimorbidity ages 45 to 59, hypertension with obesity was the most frequently occurring combination of chronic conditions among Caucasian Americans (898 [3%]) and African Americans (790 [5%]) (Table 3). Uncomplicated diabetes with hypertension was the most frequently occurring combination of chronic conditions among Asian Americans (22 [6%]) and American Indian and Alaskan Natives (9 [4%]) in this age group. Diabetes (complicated and uncomplicated) with hypertension was the most frequently occurring combination of chronic conditions among Native Hawaiian and other Pacific Islanders (23 [13%]) ages 45 to 59.

Among patients with multimorbidity ages 60 to 74, complicated diabetes with hypertension was the most frequently occurring chronic condition among Caucasian

	Table I.	Demographics	stratified by	y number	of	conditions.
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Patient demographic variables	Two chronic conditions [n = 221,792]	Three chronic conditions [n = 152,710]	Four or more chronic conditions [n = 105,659]
Number of conditions, mean	4.19 (2–22)	5.18 (3–22)	6.16 (4–22)
(range)			
Age, mean	56.87	58.87	60.44
Age, median	59	61	62
Age, mode	89	89	89
Age, range	18–105	18–105	18–105
Age, standard deviation (SD)	18.13	17.48	16.81
Age intervals, years (%)			
18–30	21722 (0.1)	11165 (0.07)	5775 (0.05)
31–44	39350 (0.18)	23908 (0.16)	14675 (0.14)
45–59	54118 (0.24)	37794 (0.25)	26264 (0.25)
60–74	66282 (0.30)	48909 (0.32)	35967 (0.34)
75–88	32924 (0.15)	25135 (0.16)	18596 (0.18)
89–105	7396 (0.03)	5799 (0.04)	4382 (0.04)
Race, number (%)		()	· · · ·
Caucasian American	138387 (0.62)	95770 (0.63)	66307 (0.63)
African American/Black	61776 (0.28)	44296 (0.29)	31747 (0.30)
Asian American	1308 (<0.00)	798 (<0.00)	507 (<0.00)
American Indian/Alaskan Native	702 (<0.00)	499 (<0.00)	373 (<0.00)
Native Hawaiian/Other Pacific Islander	611 (<0.00)	380 (<0.00)	204 (<0.00)
Other race	6965 (0.03)	4150 (0.03)	2667 (0.03)
Unknown race	12043 (0.05)	6816 (0.04)	3853 (0.04)
Ethnicity, number (%)			()
Hispanic/LatinX/Spanish	6401 (0.03)	3627 (0.02)	2246 (0.02)
Gender		()	· · · ·
Male	88683 (0.4)	61053 (0.4)	42412 (0.4)
Female	133075 (0.6)	91642 (0.6)	63239 (0.6)
Unknown	34 (<0.00)	15 (0.000)	8 (0.000)
Insurance payor, number (%)	()	((
Medicare	80795 (0.36)	63305 (0.41)	48443 (0.46)
Medicaid	34040 (0.15)	23405 (0.15)	15927 (0.15)
Blue cross Blue Shield	40154 (0.18)	25412 (0.17)	16354 (0.15)
Private insurance	40864 (0.18)	25546 (0.17)	16298 (0.15)
Unknown insurance	25939 (0.12)	15042 (0.10)	8637 (0.08)

Americans (1561 [4%]), African Americans (872 [6%]), Asian Americans (20 [6%]), and American Indian and Alaskan Natives (8 [4%]) (Table 3). In this age group, diabetes (complicated and uncomplicated) with hypertension was the most frequently occurring chronic condition among Native Hawaiian and other Pacific Islanders (23 [13%]).

Among patients with multimorbidity ages 75 to 88, uncomplicated diabetes with hypertension was the most frequently occurring combination of chronic conditions among Caucasian Americans (831 [3%]), African Americans (337 [6%]), and Asian Americans (8 [5%]) (Table 3). Congestive heart failure with hypertension was the most frequently occurring combination of chronic conditions among American Indian and Alaskan Natives (3 [5%]) in this age group. Complicated diabetes with hypertension was the most frequently occurring combination of chronic conditions among Native Hawaiian and other Pacific Islanders (3 [8%]) ages 75 to 88.

Among patients with multimorbidity ages 89 to 105, hypertension with neurological disorders was the most frequently occurring combination of chronic conditions among Caucasian Americans (170 [3%]) and uncomplicated diabetes with hypertension among African Americans (37 [3%]) (Table 3). Among Asian Americans in this age group, hypertension with neurological disorders and fluid and

Age range	Male		Female	
All ages (%) [n = 221792]	88683 (0.	4)	133075	5 (0.6)
I	DM + HTN	3267 (0.04)	HTN + OB	3788 (0.03)
2	HTN + OB	2180 (0.02)	DM + HTN	3245 (0.02)
3	DP + PSY	1416 (0.02)	DP + PSY	2866 (0.02)
4	HTN + NEU	77 (0.0)	DP + HTN	1949 (0.01)
5	HTN + TU	1070 (0.01)	DP + OB	1106 (0.01)
18–30, (0.10) [n = 21722]	5982 (0.2	8)	15737	
I	DP + PSY	678 (0.11)	DP + PSY	1182 (0.08)
2	HTN + OB	151 (0.03)	ANE + BL	549 (0.03)
3	CP + OB	135 (0.02)	DP + OB	514 (0.03)
4	DP + DG + PSY	133 (0.02)	HTN + OB	486 (0.03)
5	DG + PSY	130 (0.02)	DP + OB + PSY	305 (0.02)
31–44, (0.18) [n = 39350]	12786 (0.3		26557	
1	HTN + OB	502 (0.04)	HTN + OB	1182 (0.04)
2	DP + PSY	414 (0.03)	DP + PSY	848 (0.03)
3	DM + HTN	217 (0.02)	DP + OB	592 (0.02)
4	DG + PSY	210 (0.02)	ANE + BL	418 (0.02)
	DP + HTN	192 (0.01)	DP + HTN	415 (0.02)
45–59, (0.24) [<i>n</i> = 54118]	22909 (0.4		31203	
	DM + HTN	999 (0.04)	HTN + OB	1104 (0.04)
2	HTN + OB	790 (0.03)	DM + HTN	816 (0.03)
3	DM + DMC + HTN	324 (0.01)	DP + HTN	603 (0.02)
4	DP + HTN	321 (0.01)	DP + PSY	447 (0.01)
5	DM + HTN + OB	310 (0.01)	DP + HTN + OB	310 (0.01)
60–74, (0.30) [<i>n</i> = 66282]	30262 (0.4		36014	
	DM + HTN	1400 (0.05)	DM + HTN	1342 (0.04)
2	HTN + OB	643 (0.02)	HTN + OB	857 (0.02)
3	HTN + TU	530 (0.02)	DP + HTN	616 (0.02)
4	DM + DMC + HTN	371 (0.01)	HTN + HY	470 (0.01)
5	HTN + NEU	335 (0.01)	HTN + TU	392 (0.01)
75–88, (0.15) [<i>n</i> = 32924]	14397 (0.4		18523	. ,
	DM + HTN	579 (0.04)	DM + HTN	615 (0.03)
2	HTN + TU	329 (0.02)	HTN + HY	328 (0.02)
3	HTN + NEU	319 (0.02)	HTN + NEU	321 (0.02)
4	DM + DMC + HTN	150 (0.01)	HTN + TU	298 (0.2)
5	HTN + PER	145 (0.01)	DP + HTN	169 (0.01)
89–105, (0.03) [n = 7396]	2347 (0.3		5041 (()
	HTN + NEU	64 (0.03)	HTN + NEU	144 (0.03)
2	DM + HTN	43 (0.02)	HTN + HY	(0.02)
3	HTN + TU	40 (0.02)	DM + HTN	97 (0.02)
4	CHF + HTN	34 (0.01)	CHF + HTN	70 (0.01)
5	METS + TU	26 (0.01)	HTN + TU	51 (0.01)
		20 (0.01)		51 (0.01)

Table 2. Most frequent combinations of chronic conditions stratified by age and gender.

*ANE = anemia deficiency; BL = blood loss anemia; CHF = congestive heart failure; CP = chronic pulmonary disease; DG = Drug abuse; DM = diabetes, uncomplicated; DMC = diabetes, complicated; DP = depression; HTN = hypertension, complicated; METS = metastatic cancer; NEU = neurological disorders; OB = obesity; PER = peripheral vascular disorders; PSY = psychoses; TU = solid tumor without metastasis. **Participants with unknown gender were excluded from this table because they represented less than 1% (n = 34) of the study population.

electrolyte disorders was the most frequently occurring combination of chronic conditions (2 [5%]). Among American Indian and Alaskan Natives ages 89 to 105, hypertension with metastatic cancer was the most frequently occurring combination of chronic conditions (1 [25%]). Table 4 reflects additional categories of race (i.e., other race, unknown race) and ethnicity. The category of "other race" represents patients of non-American nationality (e.g., of African descent, but not "African American," of Asian descent but not "Asian American"). For all ages,

	Caucasian American		African America	n	Asian American		American India Alaskan native	n/	Native Hawaiiar Islander	ı/Pacific
				All	ages, number (%)	, [n = 22	I 792]			
	138386	(0.62)	61776 (0.	28)	1308 (0.0	I)	702 (<0.	00)	611 (<0.)0)
I	DM + HTN	3615 (0.03)	HTN + OB	2430 (0.04)	DM + HTN	56 (0.04)	DM + HTN	24 (0.04)	DM + DMC + HTN	56 (0.09
2	HTN + OB	2924 (0.02)	DM + HTN	2062 (0.03)	DP + PSY	41 (0.03)	HTN + OB	15 (0.02)	DM + DMC	48 (0.08
;	DP + PSY	2749 (0.02)	DP + PSY	820 (0.01)	HTN + OB	34 (0.03)	ANE + BL	10 (0.01)	DM + HTN	34 (0.06
	DP + HTN	1566 (0.01)	DP + HTN	593 (0.01)	ANE + BL	23 (0.02)	DP + PSY	10 (0.01)	DMC + HTN	25 (0.04
•	HTN + TU	1425 (0.01)	DM + HTN + OB	543 (0.01)	HTN + LIV	16 (0.01)	DP + OB	7 (0.01)	DM + DMC + HTN + OB	16 (0.03
				A	Ages: 18–30, (0.10)	[n = 217	22]			
	10354	(0.48)	7917 (0.3	36)	110 (0.01)	72 (<0.0	0)	36 (<0.0	0)
I	DP + PSY	24 (0.)	DP + PSY	475 (0.06)	DP + PSY	7 (0. 5)	DP + PSY	4 (0.05)	ANE + BL	4 (0.11
	htn + Ob	255 (0.02)	HTN + OB	284 (0.04)	DP + OB	4 (0.04)	CP + OB	3 (0.04)	DMC + HTN	2 (0.05
	DP + OB	(0.02)	ANE + BL	252 (0.03)	HY + OB	3 (0.03)	HTN + OB	3 (0.04)	ANE + BL + COA + DM	2 (0.05
	DP + NEU	194 (0.02)	DP + OB	160 (0.02)	CP + DP + PSY	3 (0.03)	ANE + BL	2 (0.03)	DP + PSY	2 (0.05
5	DP + DG	183 (0.02)	DP + OB+ PSY	116 (0.01)	ANE + BL	3 (0.03)	DP + OB	2 (0.03)	BL + OB	2 (0.05)
				A	Ages: 31–44, (0.18)	[n = 393	50]			
21058 (0.54)		(0.54)	13611 (0.	35)	331 (0.01)		160 (<0.00)		131(<0.00)	
l	DP + PSY	822 (0.04)	HTN + OB	823 (0.06)	ANE + BL	20 (0.06)	ANE + BL	8 (0.05)	DM + DMC	19 (0.15
2	HTN + OB	668 (0.03)	DP + PSY	229 (0.02)	DP + PSY	l7 (0.05)	DP + OB	5 (0.03)	DM + HTN	8 (0.06
3	DP + NEU	366 (0.02)	DP + HTN	213 (0.02)	HTN + OB	10 (0.03)	DP + PSY	4 (0.03)	DM + OB	6 (0.05
ł	DP + OB	336 (0.02)	DP + OB	190 (0.01)	HY + OB	6 (0.02)	DM + HTN	4 (0.03)	HTN + OB	6 (0.05
5	DP + HTN	325 (0.02)	DM + HTN	189 (0.01)	CP + DP	5 (0.01)	HTN + LYT	3 (0.02)	DM + DMC + OB	5 (0.04
				А	ages: 45–59, (0.24),	[n = 541	18]			
	32268	(0.6)	16736 (0.	31)	342 (0.01)	214 (<0.	00)	223 (<0.)0)
	HTN + OB	898 (0.03)	HTN + OB	790 (0.05)	DM + HTN	22 (0.06)	DM + HTN	9 (0.04)	DM + DMC + HTN	28 (0.13

Table 3. Most frequent combinations of chronic conditions stratified by age and race.

(continued)

ΗY

5 HTN +

OB

(0.01)

(0.01)

181

 Table 3. (continued)

	Caucasian American		African America	ın	Asian American		American India Alaskan native	n/	Native Hawaiian Islander	/Pacific
3	DP + HTN	565 (0.02)	DP + HTN	228 (0.01)	METS + TU	8 (0.02)	HTN + OB	4 (0.02)	DM + HTN	10 (0.04)
4	DP +	485	DM + DMC +	188	HTN + HY	6	METS + TU	3	DMC + HTN	9
	PSY	(0.02)	HTN	(0.01)		(0.02)		(0.01)		(0.04)
5	DP +	297	HTN + LYT	183	HY + TU	5	DP + DG +	3	DM + DMC +	8
	NEU	(0.01)		(0.01)		(0.01)	HTN + PSY	(0.01)	HTN + OB	(0.04)
				A	ges: 60–74, (0.30),	n = 662	282]			
	44117	(0.67)	16854 (0	.25)	337 (0.01)		196 (<0.	00)	181 (<0.0	0)
I	DM + HTN	56 (0.04)	DM + HTN	872 (0.06)	DM + HTN	20 (0.06)	DM + HTN	8 (0.04)	DM + DMC + HTN	23 (0.13)
2	HTN + OB	913 (0.02)	HTN + OB	483 (0.03)	DP + HTN	7 (0.02)	HTN + OB	5 (0.02)	DM + HTN	l 3 (0.07)
3	HTN + TU	678 (0.02)	HTN + TU	190 (0.01)	DM + DMC + HTN	7 (0.02)	HTN + TU	4 (0.02)	DMC + HTN	 (0.06)
4	DP + HTN	450 (0.01)	DM + HTN + OB	187 (0.01)	HTN + OB	7 (0.02)	HTN + REN	2 (0.01)	DMC + HTN + REN	6 (0.03)
5	METS + TU	398 (0.01)	DM + DMC + HTN + OB	162 (0.01)	HTN + LYT	6 (0.02)	HTN + OB + TU	2 (0.01)	DM + DMC	5 (0.02)
				A	ges: 75–88, (0.15),	n = 329	924]			
	25049	(0.76)	5455 (0.	17)	151 (<0.00)	57 (<0.0	0)	38(<0.00))
I	DM + HTN	831 (0.03)	DM + HTN	337 (0.06)	DM + HTN	8 (0.05)	CHF + HTN	3 (0.05)	DMC + HTN	3 (0.08)
2	HTN + NEU	(0.03) 554 (0.02)	HTN + TU	66 (0.01)	HTN + LIV	(0.03) 3 (0.02)	DM + HTN	(0.03) I (0.02)	DM + HTN	(0.00) 3 (0.08)
3	HTN + TU	535 (0.02)	HTN + NEU	58 (0.01)	DM + HTN + REN	· /	NEU + TU	(0.02) I (0.02)	HTN + HY	2 (0.05)
4	HTN +	259	HTN + OB	47	DM + DMC	2	LYT + NEU +		HTN + PER	2

Ages: 89-105 (0.03), [n = 7396]

HTN + PAR

(0.01)

(0.01)

2

PAR

HTN + PAR

(0.02)

(0.02)

T

HTN + REN

(0.05)

(0.03)

Т

(0.01)

(0.01)

43

DM + HTN +

ΤU

	5540 ((0.75)	1203 (0.	16)	37 (<0.00)		4 (<0.0	0)	2 (<0.00))
I	HTN + NEU	170 (0.03)	DM + HTN	37 (0.03)	HTN + LYT + NEU	2 (0.05)	HTN + MET	l (0.25)	ANE + CHF + HY + REN	l (0.05)
2	HTN + HY	93 (0.02)	HTN + NEU	17 (0.01)	DM + DMC	2 (0.05)	HTN + LIV + REN + TU	l (0.25)	HTN + TU	í (0.05)
3	DM + HTN	86 (0.02)	ANE + HTN	9 (0.01)	PER + TU	l (0.03)	DM + HTN	l (0.25)		
4	CHF + HTN	85 (0.02)	HTN + OB	9 (0.01)	HTN + LYT + REN	l (0.03)	HTN + NEU	l (0.25)		
5	HTN + TU	80 (0.01)	CHF + HTN	8 (0.01)	HTN + LYT + NEU + REN + TU	l (0.03)		. ,		

*ANE = anemia deficiency; BL = blood loss anemia; CHF = congestive heart failure; COA = coagulopathy; CP = chronic pulmonary disease; DP = depression; DM = uncomplicated diabetes; DMC = complicated diabetes; DG = drug abuse; HTN = complicated hypertension; HY = hypothyroidism; LIV = liver disease; LYT = fluid and electrolyte disorders; METS = metastatic cancer; NEU = neurological disorders; OB = obesity; PAR = paralysis; PER = peripheral vascular disorders; PSY = psychoses; REN = renal failure; TU = solid tumor without metastasis; VAL = valvular disease.

Rank	Other race		Unknown race	9	Ethnicity, Hispanic/Lat	inX/Spanish
		All ages, number	· (%), [n = 221]	792]		
	6965 (0.03)		12043 (0.05)		6410 (0.03)	
I	DM + HTŃ	263 (0.04)	DP + PSY	508 (0.04)	DM + HTŃ	248 (0.04)
2	ANE + BL	250 (0.04)	DM + HTN	460 (0.04)	ANE + BL	230 (0.04)
3	HTN + OB	178 (0.03)	HTN + OB	378 (0.03)	HTN + OB	197 (0.03)
4	DP + PSY	151 (0.02)	CP + HTN	230 (0.02)	DP + PSY	193 (0.03)
5	DM + OB	82 (0.01)	DP + HTN	228 (0.02)	DM + OB	99 (0.02)
		Ages: 18–30, (0	0.10) [n = 2172	2]		
	387 (0.06)		1846 (0.08)		1525 (0.05)	
I	ANE + BL	138 (0.1)	DP + PSY	269 (0.15)	ANE + BL	134 (0.09)
2	DP + PSY	83 (0.06)	CP + DP	96 (0.05)	DP + PSY	123 (0.08)
3	ANE + BL + OB	33 (0.02)	HTN + OB	62 (0.03)	DP + OB	46 (0.03)
4	DP + OB	33 (0.02)	DP + OB	61 (0.03)	HTN + OB	41 (0.03)
5	HTN + OB	31 (0.02)	CP + OB	42 (0.03)	BL + OB	35 (0.02)
		Ages: 31-44, (0).18) [n = 3935	0]		
	2045 (0.05)		2015 (0.05)		1989 (0.05)	
I	ANE + BL	112 (0.05)	DP + PSY	145 (0.07)	ANE + BL	96 (0.05)
2	HTN + OB	72 (0.04)	HTN + OB	104 (0.05)	HTN + OB	82 (0.04)
3	DM + OB	50 (0.03)	DP + OB	58 (0.03)	DM + OB	57 (0.03)
4	DM + HTN	47 (0.03)	DP + HTN	51 (0.03)	DP + PSY	47 (0.02)
5	DP + PSY	43 (0.03)	DM + HTN	51 (0.03)	DM + HTN	46 (0.02)
		Ages: 45-59, (0	.24), [n = 5411	8]		
	1664 (0.03)		2670 (0.05)		1520 (0.03)	
I	DM + HTN	106 (0.06)	HTN + OB	130 (0.05)	DM + HTN	108 (0.07)
2	HTN + OB	51 (0.03)	DM + HTN	114 (0.04)	HTN + OB	52 (0.03)
3	DM + DMC	26 (0.02)	DP + HTN	93 (0.03)	DM + DMC + HTN	42 (0.02)
4	DM + DMC + HTN	24 (0.01)	DP + PSY	60 (0.02)	DM + DMC	29 (0.03)
5	DP + HTN	20 (0.01)	CP + HTN	53 (0.02)	DP + HTN	18 (0.01)
		Ages: 60-74, (0	.30), [<i>n</i> = 6628	2]		
	1297 (0.02)		3300 (0.05)		981 (0.01)	
I	DM + HTN	103 (0.06)	DM + HTN	196 (0.06)	DM + HTN	71 (0.07)
2	HTN + OB	22 (0.02)	CP + HTN	104 (0.03)	DM + DMC + HTN	21 (0.02)
3	DM + DMC + HTN	19 (0.01)	METS + TU	86 (0.03)	HTN + OB	18 (0.02)
4	DM + HTN + OB	16 (0.01)	HTN + OB	71 (0.02)	HTN + TU	12 (0.01)
5	DMC + HTN	15 (0.01)	DP + HTN	51 (0.02)	HTN + LIV	(0.0)
		Ages: 75-88, (0	.15), [n = 3292	.4]		
	477 (0.01)		1697 (0.05)		314 (0.19)	
I	DM + HTN	24 (0.05)	DM + HTN	75 (0.04)	DM + HTN	11 (0.03)
2	HTN + HY	8 (0.02)	METS + TU	52 (0.03)	DM + DMC + HTN	6 (0.02)
3	HTN + LYT	7 (0.01)	CP + HTN	34 (0.02)	DMC + HTN	4 (0.01)
4	DM + DMC + HTN	6 (0.01)	HTN + HY	31 (0.02)	HTN + LYT	4 (0.01)
5	HTN + PAR	5 (0.01)	HTN + TU	23 (0.01)	HTN + REN	4 (0.01)

Table 4. Most frequent combinations of chronic conditions stratif	ied by age, unknown race, and ethnicity.
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(continued)

Rank	Other race	ace Unknown race				Ethnicity, Hispanic/LatinX/Spanish					
	Ages: 89–105, (0.03), [n = 7396]										
	95 (0.01)		515 (0.07)		81 (0.01)						
I I	DM + HTN	4 (0.04)	HTN + NEU	16 (0.03)	DM + HTN	2 (0.02)					
2	HTN + NEU	4 (0.04)	DM + HTN	11 (0.02)	NEU + ULC	1 (0.01)					
3	HTN + LYT	2 (0.02)	HTN + PER	10 (0.02)	NEU + TU	1 (0.01)					
4	HTN + HY + LYT + NEU	2 (0.02)	CHF + HTN	9 (0.02)	HTN + REN	1 (0.01)					
5	ANE + COA + HTN + HY + LYT + TU	1 (0.01)	HTN + LYT	9 (0.02)	HTN + LYT	I (0.01)					

Table 4. (continued)

*ANE = anemia deficiency; BL = blood loss anemia; CHF = congestive heart failure; COA = coagulopathy; CP = chronic pulmonary disease; DP = depression; DM = diabetes, uncomplicated; DMC = diabetes, complicated; HTN = hypertension, complicated; HY = hypothyroidism; LIV = liver disease; LYT = fluid and electrolyte disorders; METS = metastatic cancer; NEU = neurological disorders; OB = obesity; PAR = paralysis; PER = peripheral vascular disorders; PSY = psychoses; TU = solid tumor without metastasis; ULC = peptic ulcer disease.

uncomplicated diabetes with hypertension was the most frequently occurring combination of chronic conditions among patients of other race (263 [4%]) and Hispanic, LatinX, and Spanish ethnicity (248 [4%]). Depression with psychoses was the most frequently occurring combination of chronic conditions among all ages of patients of unknown race (508 [4%]).

Among patients with multimorbidity ages 18 to 30, anemia deficiency with blood loss anemia was the most frequently occurring combination of chronic conditions among patients of other race (138 [1%]) and those of Hispanic, LatinX, and Spanish ethnicity (134 [9%]) (Table 4). Depression with psychoses was the most frequently occurring combination of chronic conditions among patients with multimorbidity of unknown race in this age group (269 [15%]).

Among patients with multimorbidity ages 31 to 44, anemia deficiency with blood loss anemia was the most frequently occurring combination of chronic conditions among patients of other race (112 [5%]) and those of Hispanic, LatinX, and Spanish ethnicity (96 [5%]) patients with multimorbidity (Table 4). In the same age group, depression with psychoses was the most frequently occurring combination of chronic conditions among patients of unknown race (145 [7%]).

Among patients with multimorbidity ages 45 to 59, uncomplicated diabetes with hypertension was the most frequently occurring combination of chronic conditions among patients of other race (106 [6%]) and those of Hispanic, LatinX, and Spanish ethnicity (108 [7%]) (Table 4). Within the same age group, hypertension with obesity was the most frequently occurring combination of chronic conditions among patients of unknown race (130 [5%]).

Among patients with multimorbidity ages 60 to 74, uncomplicated diabetes with hypertension was the most frequently occurring combination of chronic conditions among patients of other race (103 [6%]), Hispanic, LatinX, and Spanish ethnicity (71 [7%]), and unknown race (196 [6%]) (Table 4).

Among patients with multimorbidity ages 75 to 88, uncomplicated diabetes with hypertension was the most frequently occurring combination of chronic conditions among patients of other race (24 [5%]), Hispanic, LatinX, and Spanish ethnicity (11 [3%]), and unknown race (75 [4%]) (Table 4).

Among patients with multimorbidity ages 89 to 105, uncomplicated diabetes with hypertension was the most frequently occurring combination of chronic conditions among patients of other race (4 [4%]) and those of Hispanic, LatinX, and Spanish ethnicity (2 [2%]) (Table 4). Among patients of unknown race in this age group, hypertension with neurological disorders was the most frequently occurring combination of chronic conditions (16 [3%]).

Discussion

The study characterized patterns of multimorbidity across patients. Subsequently, the study assessed the informatics capacity (technologies, data, processes, etc.) of a learning health system, using the AR-CDR as a use case. The study found multimorbidity was highest among patients ages 60 to 74, Caucasians, females, and Medicare payors. The largest numbers of chronic conditions occurred in the smallest numbers of patients with multimorbidity (i.e., 70,262 (31%) patients with two conditions, two (<1%) patients with 22 chronic conditions). Patients from racially underrepresented groups have been consistently shown to have the highest rates of mortality and have had lower rates of insurance coverage before becoming Medicare age-eligible.^{8–13} Age has been of consistent interest in monitoring the expansion of disease accumulation throughout the lifespan,³⁵ grounded in the accumulation of chronic conditions throughout the lifespan.

Broadly, the results revealed that the LHS's captured data supported the characterization of multimorbidity across patients through the stratification of multimorbidity patient data among demographic variables (i.e., age, race, ethnicity, gender, and insurance). However, the study revealed several urgent needs (detailed longitudinal tracking of compounded diagnoses, additional data elements, etc.) to expand the LHS's informatics capacity.

Differences in chronic disease patterns

Over 40 studies estimated the national prevalence of multimorbidity ranged from 13% in adults ages 18 and older to 95% in populations ages 65 and older.^{35,36} Broadly, the results were consistent with similar studies conducted between 1988 and 2018.^{35–37} However, significant differences in chronic disease patterns were identified. Importantly, the combinations of most frequently occurring conditions combinations differed from national estimates.³⁸⁻⁴⁰ More specifically, uncomplicated diabetes with hypertension was the most frequently occurring combination of chronic conditions identified among all patients with multimorbidity (6514 patients [6%]). Diabetes and hypertension were also largely represented in secondary and tertiary patterns that were identified. Data from the Behavioral Risk Factor Surveillance System (n = 450,462) estimated the combination of hyperlipidemia and hypertension as the most frequently occurring combination in Arkansas.⁶ An analysis of data from the National Health Interview Survey (n =166,126) estimated the most frequently occurring multimorbidity combinations were a dyad of arthritis with hypertension and the triad of arthritis with hypertension and diabetes.² A study of *Medical Expenditure Panel Survey* data (n = 24,870) found the most frequently occurring dyad was hypertension with hyperlipidemia and a triad of diabetes, hypertension, and hyperlipidemia.³⁹ A study of National Ambulatory Medical Care Survey data (n =36,697) found the most frequent dyad was hypertension with hyperlipidemia and a triad of hypertension with hyperlipidemia and diabetes.⁴⁰ Within these national estimates, hyperlipidemia was a notable difference when compared against the actual disease occurrences identified in this study. Yet, collectively, these national estimates of occurrences (diabetes, hypertension, hyperlipidemia, etc.) have contributed to Arkansas' reputation as a member of the "Stroke-belt" [States with high stroke mortality rates].^{40,41} Diabetes, hypertension, and hyperlipidemia are commonly co-occurring in patients,^{42,43} a consistently identified characteristic of many non-communicable, chronic diseases patterns with similar risk behaviors (e.g., nutrition, physical activity, and smoking habits). Yet, patterns of chronic disease remain much less predictable than communicable diseases which follow clearer patterns of spreading across populations through disease carrying agents.⁴⁴ Chronic disease patterns will remain unelucidated without future examinations of the risk factors (i.e., psycho-social, cultural, ethnic, and socioeconomic attributes of populations) that

underpin chronic diseases accumulation .⁴⁴ Furthermore, clinical information systems must expand data collection efforts to include risk factor data. Patient assessments performed by clinical teams at the point-of-care can no longer continue to exist in isolation with linear foci on collecting physiological data (e.g., temperature, heart rate, glucose levels, and blood pressure), alone, largely due to our reliance on using population-level research to address risk factors. However, the amelioration of chronic diseases can more comprehensively be addressed by intersecting clinical and public health domains to cultivate informatics' capacity

Cultivating informatics capacity in the LHS

to improve patient outcomes.

Findings revealed an array of chronic condition combinations within multimorbidity. This emphasizes the need for healthcare systems to simultaneously provide care for both the diverse, routine care needs of multimorbidity (e.g., noncommunicable diseases) that can be anticipated and facilitate the variability of unplanned care encounters that are needed during such times as large-scale, communicable disease outbreaks.³⁰ Complicatedly, medical care (e.g., clinical guidelines and therapeutics) has been traditionally siloed into single disease processes, not the complex interplay of multiple medical conditions [and multiple social conditions, for that matter].¹⁹ This has significantly limited the data that is currently captured. Historically, data elements are the primary support mechanisms for clinical research (i.e., Charlson Comorbidity Index, Elixhauser Score) and improvements in population health.^{45,46} Most significantly, this provides an opportunity for creating more structured, multimorbidity-centric data elements that are collected and collated in EHR systems. New data elements, fueled by clinical assessments, could include a dichotomous classification of each patient as "multimorbid." Further, within EHR systems, there is a need for more enhanced processes of detailed, longitudinal tracking of initial chronic diagnoses and subsequent chronic conditions as they are compounded. For example, African American patients were more likely to have hypertension and obesity at an earlier age (i.e., 31-44) than their Caucasian American counterparts. However, the lack of multimorbidity data elements inhibited the use of the EHR to trigger flags when an African American patient crosses a multimorbidity age-related, risk threshold. These additional multimorbidity data elements could better position care systems to address health equity across the life span. Furthermore, additional data elements could prevent multimorbidity patients from converting to the highest cost tier, decreasing the overall cost of healthcare in the US.

Additional data elements would provide the infrastructure required to integrate recent advancements in informatics such as the use of clinical data registries.^{46,47} Clinical data registries serve as primary databases of aggregated, longitudinal health data (i.e., patient characteristics, treatment patterns, and clinical outcomes) related to specific conditions.^{46,48} Registries aggregate data from EHR systems at local, regional, and national levels.⁴⁹ First, the informatics infrastructure of existing clinical data registries focused on single conditions could be enhanced to support the extracting and sharing of data from multiple disease registries for use in multimorbidity research. In contrast, consolidated datasets cannot be easily obtained and aggregated from other sources, suggesting a need to formalize a registry for multimorbidity. Unfortunately, there are no known clinical data registries that explicitly target multimorbidity without being confined by the lens of single, chronic conditions (e.g., cancer, diabetes, and stroke).

Furthermore, the establishment of clinical data registries facilitates the adoption of emerging data standards for linking clinical data registries with EHR systems.⁴⁶ Data standards assist with automating the exchange and reuse of data between EHR systems and clinical data registries.⁴⁶ For example, the integration of the new Fast Healthcare Interoperability Resources (FHIR®) data standard would advance the meaning and format of new, structured data elements collected in EHR systems.⁴⁶ Integrating FHIR, in conjunction with new data elements and a new multimorbidity-centered clinical data registry could improve point-of-care feedback loops within LHS, providing real world evidence from real world data to clinical teams.^{47,49,50} Fueling feedback loops with these recent advances in informatics could reveal how patients are preforming, nationally, in the combination of single, chronic conditions that compose multimorbidity (e.g., HbA1c, lipid, and systolic/diastolic levels in diabetes, hyperlipidemia, and hypertension, respectively).⁵⁰ These advances provide a pathway for improving EHR utility to the LHS and respond to national calls for embedding data standards clinical research in informatics.⁴⁸ This maximizes the utilization of those with the highest spend in healthcare (i.e., 50% of healthcare spend is in the top 5% of multimorbidity patients), generating elasticity that could ensure stability of a health care system when balancing routine and critical care needs.²¹ Further, understanding multimorbidity patients (and those that worsen) versus those that are static can provide insight into healthcare systems. Without more multimorbid-centric informatics infrastructure (e.g., data elements, standards, and registries), clinical data cannot be maximized for use in the clinical and population research that strengthens the LHS.

Limitations

Study data were generated from Arkansas' only academic medical center, which provides care for patients throughout the entire state of Arkansas. However, this academic health center setting may be more diverse than smaller, non-academic health

centers that provide care throughout the State. Findings may not be generalizable to the larger population of individuals living with multimorbidity in the region.

Conclusion

Learning health systems for multimorbidity have the capacity to characterize patterns of multimorbidity among an array of demographic groups (i.e., age, gender, race, and ethnicity) with ease. However, learning health systems are constrained by current technologies, data elements, and data-capturing processes. As a next step, more structured multimorbidity-centric, data elements must be created in EHR systems (i.e., dichotomous classifications of patients as "multimorbid," longitudinal tracking of initial chronic disease diagnoses and subsequent chronic conditions as they compound). Finally, robust socio-technical system studies of clinical workflows are needed to assess the feasibility of integrating the collection of risk factor data elements (i.e., psycho-social, cultural, ethnic, and socioeconomic attributes of populations) into primary care encounters that patients have with healthcare systems. These approaches to advancing learning health systems for multimorbidity could substantially reduce the constraints of current technologies, data elements, and data-capturing processes. Without additional capacity for collecting and aggregating large-scale data, multimorbidity patients cannot benefit from the recent advancements in informatics (i.e., clinical data registries, emerging data standards) that are abundantly working to improve the care outcomes of patients with single chronic conditions.

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