Undiagnosed HIV and HCV in a New York City Emergency Room, 2015

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Background

Undiagnosed HIV and HCV infection represent missed opportunities for care, treatment and prevention of secondary transmission. CDC estimates that 13% of HIV-infected and 50% of HCV-infected persons nationwide are undiagnosed and unaware of their infection. We sought to measure the prevalence of HIV and HCV, the proportion undiagnosed/unaware, and the proportion coinfected in persons presenting to a busy NYC emergency room in 2015.

Methods: *Specimen Salvage and Data Matching*

Design: Cross-sectional blinded serosurvey.

Specimen source: Remnant serum from consecutive chemistry specimens drawn March 8, 2015-May 8, 2015, for clinical indications other than HIV testing in the emergency room.

Data sources: Central Laboratory Information Management Systems, Hospital Electronic Medical Record (EMR), HIV Surveillance Registry, HCV Surveillance Registry.

Process: Salvage serum, deduplicate; match to hospital EMR for demographic and clinical data; match to HIV and HCV surveillance registries for diagnosed HIV and HCV.

Analysis: Calculate overall prevalence (N positive/total N tested), prevalence of undiagnosed infection (N undiagnosed/total N tested), proportion undiagnosed (N undiagnosed/N positive), number needed to test (NNTT) to detect one previously undiagnosed (total N tested/N undiagnosed).

Laboratory Methods: *Delinking and Testing*

Removal of personal identifiers: All names, exact dates of birth, exact dates of admission to emergency room, medical record numbers, and any other identifiers were permanently removed from the serosurvey database.

Specimen source: The first consecutive 5,004 specimens appearing to have sufficient remnant serum to complete the 2- or 3-step testing algorithm for HIV or HCV were selected and transferred to the laboratory.

HIV and HCV testing algorithms: Standard clinical testing algorithms were used to ascertain HIV and HCV antibody/RNA status and infection. Testing was performed by Quest Diagnostics, Inc., at their San Juan Capistrano, CA, facility.

Laboratory Methods: *HIV Testing*

Screening: 4th generation combination Antigen-Antibody immunoassay (Architect® HIV Ag/Ab Combo, Abbott Laboratories, Lake Bluff, IL).

Supplemental: 2nd generation rapid HIV-1/HIV-2 differentiation assay (BioRad Multispot® HIV-1/HIV-2 Rapid Test, BioRad Laboratories, Redmond, WA).

Resolution of HIV-1 RNA status of specimens that were repeatedly reactive on screening but negative or indeterminate on supplemental testing: qualitative HIV-1 RNA Transcription-Mediated Amplification (TMA) assay (Hologic® Aptima® HIV-1 RNA Assay, Hologic Laboratories, Bedford, MA).

Laboratory Methods: *HCV Testing*

Screening: Vitros® Anti-HCV ImmunodiagnosticTest (Ortho-Clinical Diagnostics, Felindre Meadows Pencoed Bridgend, United Kingdom).

- Reactive result = signal-to-cutoff ratio of ≥ 1.0

Supplemental/Confirmatory: HCV RNA Polymerase Chain Reaction (PCR) (COBAS® Ampliprep/COBAS® TaqMan® HCV Test, version 2.0 (Roche Molecular Systems, Branchburg, NJ).

- Positive result (detected) = ≥ 15 copies of HCV RNA/ml

Table 1. HIV Prevalence, the prevalence of undiagnosed HIV and the proportion of undiagnosed HIV in an emergency department population in New York City, 2015, by demographic characteristics

			HIV-infected			HIV prevalence		Prevalence of undiagnosed HIV		Proportion of undiagnosed HIV	
			Diagnosed	Undiagnosed	Subtotal						
	N	Col %	n_1	n_2	n	n/N, % (95% CI)	P-value	n_2/N, % (95% CI)	P-value	n_2/n, % (95% CI)	P-value
Total	4,990	100.0	238	12	250	5.0 (4.4, 5.7)		0.2 (0.1, 0.4)		4.8 (2.5, 8.2)	
Sex											
Male	1,926	38.6	131	7	138	7.2 (6.1, 8.4)	<0.001	0.4 (0.2, 0.8)	0.16	5.1 (2.1, 10.2)	0.82
Female	3,064	61.4	107	5	112	3.7 (3.0, 4.4)		0.2 (0.0, 0.4)		4.5 (1.5, 10.1)	
Age											
21-29	795	15.9	18	2	20	2.5 (1.5, 3.9)	<0.001	0.3 (0.0, 0.9)	0.23	10.0 (1.2, 31.7)	0.18
30-39	768	15.4	26	1	27	3.5 (2.3, 5.1)		0.1 (0.0, 0.7)		3.7 (0.1, 19.0)	
40-49	783	15.7	50	3	53	6.8 (5.1, 8.8)		0.4 (0.0, 1.1)		5.7 (1.2, 15.7)	
50-59	984	19.7	86	4	90	9.2 (7.4, 11.1)		0.4 (0.1, 1.0)		4.4 (1.2,11.0)	
60-69	840	16.8	49	0	49	5.8 (4.4, 7.6)		0.1 (0.0, 0.4)		0.0 (0.0, 7.3)	
70-79	566	11.3	8	2	10	1.8 (0.8, 3.2)		0.4 (0.0, 1.3)		20.0 (2.5, 55.6)	
80-85	254	5.1	1	0	1	0.4 (0.0, 2.2)		0.0 (0.0, 1.4)		0.0 (0.0, 97.5)	
Race/ethnicity											
Black	1,605	32.2	110	5	115	7.2 (6.0, 8.5)	<0.001	0.3 (0.0, 0.7)	0.48	4.4 (1.4, 9.9)	0.40
Hispanic	2,663	53.4	106	5	111	4.2 (3.4, 5.0)		0.2 (0.1, 0.4)		4.5 (1.5, 10.2)	
White	318	6.4	9	0	9	2.8 (1.3, 5.3)		0.0 (0.0, 1.1)		0.0 (0.0, 33.6)	
Other/Unknown	404	8.1	13	2	15	3.7 (2.1, 6.1)		0.5 (0.1, 1.8)		13.3 (1.7, 40.5)	

CI, confidence interval; HIV, human immunodeficiency virus.

Results: *HIV*

- **308/4990** repeatedly reactive on screening
- **248** reactive on supplemental testing + two antibody-negative/RNA positive acute HIV infections **= 250 HIV+**
- **Prevalence = 5.0%** (95% CI 4.4, 5.7)
  - Male 7.2% (6.1, 8.4); Female 3.7 (3.0, 4.4)
- **Proportion undiagnosed = 4.8%** (2.5, 8.2)
- **Number needed to test (NNTT)** to detect one previously unknown positive=416 persons*

Results: *HCV*

- **Anti-HCV Antibody:** 372/4989
  - Anti-HCV prevalence = 7.5% (6.7, 8.2)
  - Proportion undiagnosed = 39.8% (34.8, 45.0)
- **HCV RNA+:** 196/4989
  - HCV RNA + prevalence = 3.9% (2.8, 5.1)
  - Proportion undiagnosed = 19.2% (11.4, 27.0)
- **NNTT** to detect one undiagnosed HCV RNA+ = 131*

Strengths

- **Availability of remnant serum**
  - Blood drawn on 63% of persons presenting to the ER (unusually high)
    - Representative prevalence estimate for this ER
      - Adequate power, NNTTs
  - Blinded testing = no consent = no bias due to differential risk perception
- **Both HIV and HCV prevalence measured**
  - Ability to measure coinfection

*Denominator for NNTT is total tested (not total minus previously diagnosed) because in the emergency room setting it is not always possible to elicit an accurate patient history

Limitations

- **HIV (1981→) and HCV (1994→) Registries**
  - Generational changes in diagnostic technology
  - Evolution of reporting standards and requirements
  - Matching surveillance registries against hospital EMR and laboratory data
- **Generalizability**
  - Bronx ER
  - All epidemics are local – serosurvey results are not representative of ERs elsewhere in NYC or ERs in US

Conclusions

- **HIV prevalence and undiagnosed proportion:** lowest in history of serosurveys in NYC ERs
- **HCV prevalence and undiagnosed proportion high**
  - Serosurvey prevalence higher than citywide estimate
  - Highest prevalence is in post WWII baby boomers
    - Prevalence also high in age 70-89 and 40-59
    - Argues against age limits in screening recommendations (now lifted in New York State)
- **Coinfection prevalent**
  - 32% of HIV+ have anti-HCV antibody
    - 21% of anti-HCV positive are HIV+
  - 16% of HIV+ are HCV RNA+
    - 19% of HCV RNA+ are HIV+

Table 2. HCV prevalence, the prevalence of undiagnosed HCV and the proportion of undiagnosed HCV in an emergency department population in New York City, 2015, by demographic characteristics

			HCV positive			HCV prevalence		Prevalence of undiagnosed HCV		Proportion of undiagnosed HCV	
			Diagnosed	Undiagnosed	Subtotal						
	N	Col %	n_1	n_2	n	n/N, % (95% CI)	P-value[a]	n_2/N, % (95% CI)	P-value[a]	n_2/n, % (95% CI)	P-value[a]
					Anti-HCV-positive						
Total	4,989	100.0	224	148	372	7.5 (6.7, 8.2)		3.0 (2.5, 3.4)		39.8 (34.8, 45.0)	
Sex											
Male	1,925	38.6	126	76	202	10.5 (9.2, 12.0)	<0.001	4.0 (3.1, 4.8)	0.00	37.6 (30.9, 44.7)	0.35
Female	3,064	61.4	98	72	170	5.6 (4.8, 6.4)		2.4 (1.8, 2.9)		42.4 (34.8, 50.2)	
Age											
21-29	796	16.0	3	13	16	2.0 (1.2, 3.2)	<0.001	1.6 (0.8, 2.5)	<0.001	81.3 (54.4, 96.0)	<0.001
30-39	770	15.4	11	11	22	2.9 (1.8, 4.3)		1.4 (0.6, 2.3)		50.0 (28.2, 71.8)	
40-49	779	15.6	26	13	39	5.0 (3.6, 6.8)		1.7 (0.8, 2.6)		33.3 (19.1, 50.2)	
50-59	984	19.7	76	36	112	11.4 (9.5, 13.5)		3.7 (2.5, 4.8)		32.1 (23.6, 41.6)	
60-69	842	16.9	82	44	126	15.0 (12.6, 17.6)		5.2 (3.7, 6.7)		34.9 (26.7, 43.9)	
70-79	564	11.3	24	25	49	8.7 (6.5, 11.3)		4.4 (2.7, 6.1)		51.0 (36.3, 65.6)	
80-85	254	5.1	2	6	8	3.2 (1.4, 6.1)		2.4 (0.5, 4.2)		75.0 (34.9, 96.8)	
Year of birth											
1929-1944	802	16.1	26	30	56	7.0 (5.3, 9.0)	<0.001	3.7 (2.4, 5.1)	<0.001	53.6 (39.7, 67.0)	0.01
1945-1965	1,904	38.2	160	82	242	12.7 (11.3, 14.3)		4.3 (3.4, 5.2)		33.9 (27.9, 40.2)	
1966-1994	2,283	45.8	38	36	74	3.2 (2.6, 4.1)		1.6 (1.1, 2.1)		48.7 (36.9, 60.6)	
Race/ethnicity											
Black	1,604	32.2	74	42	116	7.2 (6.0, 8.6)	0.58	2.6 (1.8, 3.4)	0.64	36.2 (27.5, 45.7)	0.82
Hispanic	2,665	53.4	122	86	208	7.8 (6.8, 8.9)		3.2 (2.6, 3.9)		41.4 (34.6, 48.4)	
White	316	6.3	14	10	24	7.6 (4.9, 11.1)		3.2 (1.2, 5.1)		41.7 (22.1, 63.4)	
Other/Unknown	404	8.1	14	10	24	5.9 (3.8, 8.7)		2.5 (1.0, 4.0)		41.7 (22.1, 63.4)	
					HCV RNA-positive (viral load ≥15 IU/mL)[b]						
Total	4,989	100.0	158	38	196	3.9 (2.8, 5.1)		0.8 (0.3, 1.3)		19.2 (11.4, 27.0)	
Sex											
Male	1,925	38.6	60	16	77	6.2 (4.4, 8.1)	Ref.	1.2 (0.3, 2.0)	Ref.	21.0 (11.5, 30.5)	Ref.
Female	3,064	61.4	97	22	120	2.5 (1.5, 3.5)	<0.001	0.5 (0.2, 0.9)	0.05	18.1 (7.8, 28.5)	0.64
Age											
21-29	796	16.0	0	3	3	0.4 (0.0, 0.8)	Ref.	0.3 (0.0, 0.6)[c]	Ref.	34.7 (6.3, 63.1)[c]	Ref.
30-39	770	15.4	8	2	9	1.2 (0.4, 2.1)	0.06				
40-49	779	15.6	16	2	18	2.3 (1.2, 3.5)	0.87	0.5 (0.0, 1.1)[c]	0.29	11.6 (1.7, 21.6)[c]	0.03
50-59	984	19.7	52	8	60	6.1 (3.6, 8.6)	<0.001				
60-69	842	16.9	62	15	77	9.1 (6.3, 12.0)	<0.001	1.7 (0.6, 2.9)	<0.01	18.7 (9.1, 28.4)	0.40
70-79	564	11.3	18	9	27	4.7 (2.6, 6.8)	<0.001	1.2 (0.3, 2.1)[c]	0.10	34.1 (16.2, 52.0)[c]	0.14
80-85	254	5.1	1	1	2	1.0 (0.0, 2.2)	0.14				
Year of birth											
1929-1944	802	16.1	19	9	28	3.5 (2.0, 5.1)	Ref.	1.2 (0.3, 2.0)	Ref.	33.0 (15.4, 50.6)	Ref.
1945-1965	1,904	38.2	116	23	139	7.3 (5.0, 9.6)	<0.001	1.2 (0.4, 2.0)	0.03	16.3 (8.5, 24.0)	0.17
1966-1994	2,283	45.8	22	6	28	1.2 (0.7, 1.8)	<0.001	0.3 (0.0, 0.6)	0.01	19.8 (0.2, 39.4)	0.67
Race/ethnicity											
Black	1,604	32.2	60	14	74	4.6 (3.1, 6.1)	Ref.	0.9 (0.3, 1.4)	Ref.	18.4 (9.3, 27.6)	Ref.
Hispanic	2,665	53.4	80	21	101	3.8 (2.4, 5.1)	0.70	0.8 (0.1, 1.5)	0.72	19.9 (7.2, 32.6)	0.80
White	316	6.3	8	1	9	3.0 (0.9, 5.1)	0.49	0.3	0.40	10.8 (0.0, 31.3)	0.50
Other/Unknown	404	8.1	10	3	13	3.1 (1.4, 4.8)	0.58	0.7	0.72	24.0 (0.2, 47.8)	0.50

CI, confidence interval; HCV, hepatitis C virus; IU, international unit.

[a] *P-value for anti-HCV-positive shows the overall differences between groups, and P-value for HCV-infected shows the differences compared with the reference group, because unable to combine hypothesis test results to show the overall difference with the SAS multiple imputation procedure.*

[b] *Sum may not equal total due to rounding of multiple imputation results..*

[c] *Age groups 21-29 and 30-39, 40-49 and 50-59, and 70-79 and 80-85 were collapsed due to the low number of undiagnosed HCV infections.*

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