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Chlorthalidone vs. Hydrochlorothiazide for Hypertension and Cardiovascular Events: The Diuretic Comparison Project (DCP)

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ORIGINAL ARTICLE

Chlorthalidone vs. Hydrochlorothiazide for Hypertension–Cardiovascular Events

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DCP overview

- RCT of Chlorthalidone vs HCTZ in patients with Hypertension
- Outcome – MACE and non-cancer death

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Pragmatic Nature

- All study related tasks done by central staff (Boston or Minneapolis)
- No study staff at any site
- Centralized:
  - Recruitment
  - Consenting
  - Randomization
  - Filling out drug order
  - Assessing outcomes
- Usual Care:
  - Signing drug order
  - Filling prescription
  - Managing study drug and hypertension

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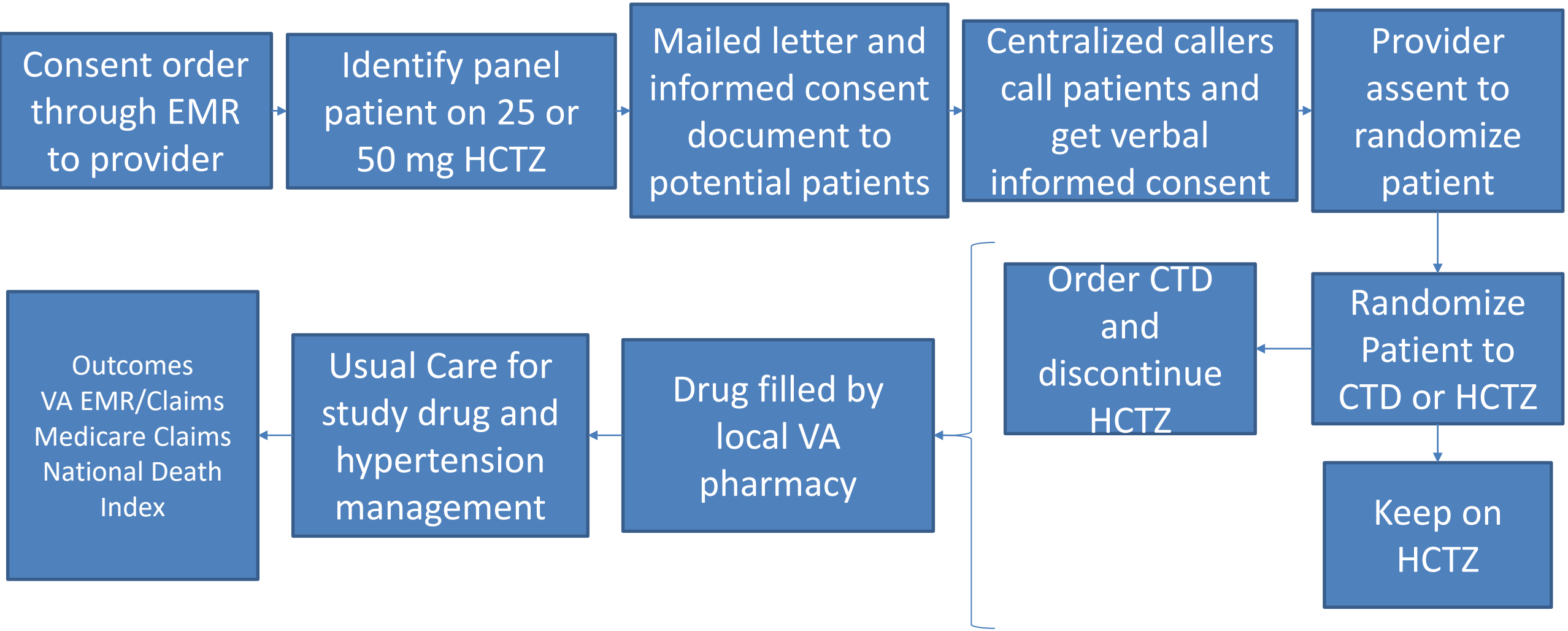
Study consent flow



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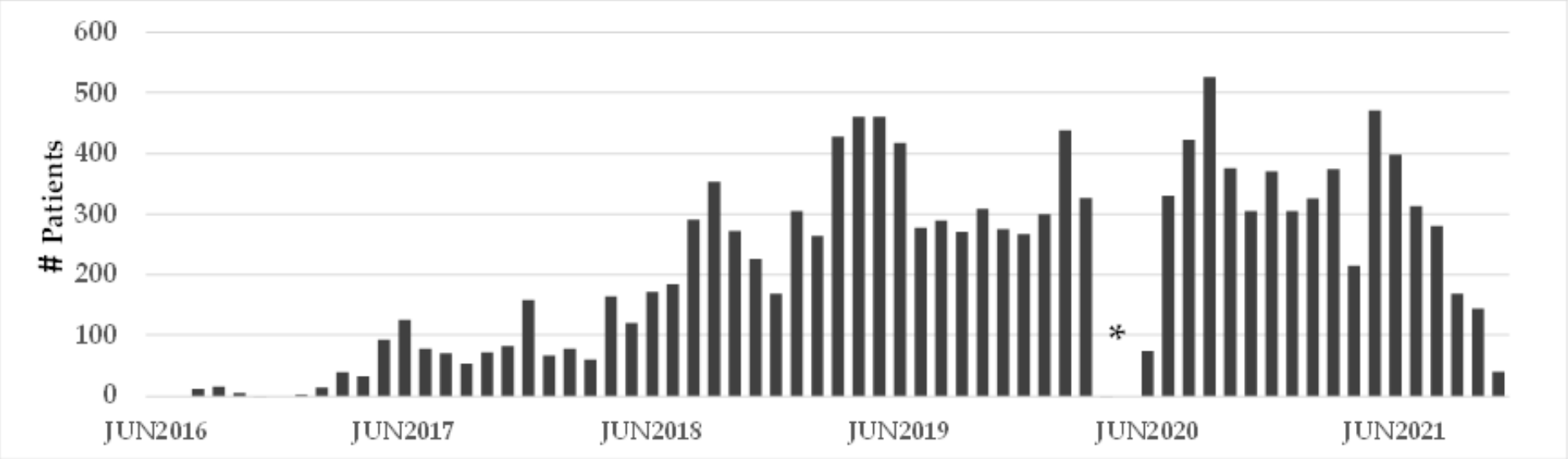
Obstacles

- Getting Facilities and providers to agree to participate
- Call Center
  - Initially contracted with existing VA call center
  - No prior research experience
  - They had other priorities
- Mid study – started our own dedicated call center in Minneapolis
- COVID

Figure 4. Recruitment Results for the Diuretic Comparison Project (DCP)

	Cumulative Number of VA Primary Care Networks	Yearly Randomized rate (Monthly average)
Jun - Dec 2016	1	31 (4)
Jan - Dec 2017	5	812 (68)
Jan - Dec 2018	23	2,153 (179)
Jan - Dec 2019	52	4,020 (335)
Jan - Dec 2020	66	3,470 (289)
Jan - Nov 2021	72	3,037 (276)

Monthly Randomization Rate from June 2016 to November 2021

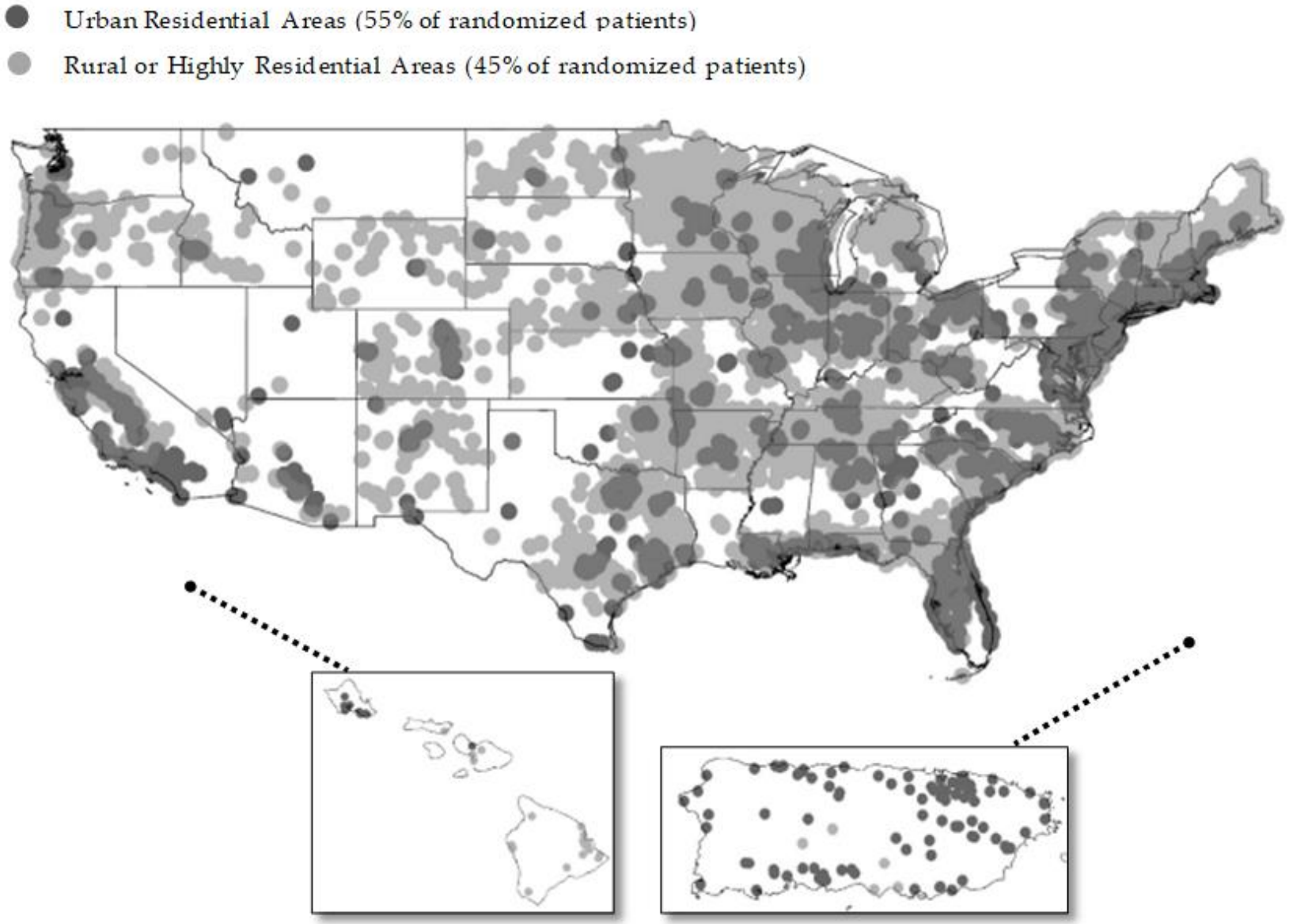


*Recruitment activity was temporary suspended due to COVID-19 pandemic

Benefits of waiver of documentation of informed consent

- Broad based participation
- 14.9% Black and 7.7% non White or black’
- 45% Rural
  - 1.5% Highly rural
- Inclusion of sites/providers that never participate in research

Figure 3. Geographic Distribution of Randomized Patients across the United States (N = 13,523) [1,2]



[1] There were 55 patients from Alaska and 39 patients from the District of Columbia (not displayed in the figure)
[2] MAP not drawn to actual proportions

								Consented		Eligible for randomization		Randomized	
#	Site#	Site Launch Date	Patients identified	Failed pre-screen	Qualified pre-screen	Completed contact	Expected randomized [3]	n	% of expected	n	% of expected	n	% of expected
	Overall		**1,399,571**	**1,331,984**	**67,587**	**42,487**	**23,682**	**16,276**	**68.7%**	**13,449**	**56.8%**	**13,232**	**55.9%**
1	Boston	06/17/2016	16,091	15,248	843	731	296	153	51.7%	135	45.6%	135	45.6%
2	MSP	01/19/2017	47,533	44,676	2,857	2,451	1,000	832	83.2%	735	73.5%	733	73.3%
3	614	04/26/2017	21,517	20,291	1,226	1,019	430	251	58.4%	216	50.2%	212	49.3%
4	LA	07/01/2017	30,340	29,034	1,306	1,061	457	254	55.6%	198	43.3%	197	43.1%
5	541	10/18/2017	50,024	47,425	2,599	2,119	910	466	51.2%	377	41.4%	375	41.2%
6	578	01/17/2018	20,964	19,789	1,175	946	412	241	58.5%	203	49.3%	201	48.8%
7	Portland	03/2018	29,025	27,630	1,395	1,104	489	408	83.4%	342	69.9%	339	69.3%
8	600	03/15/2018	17,479	16,859	620	441	217	128	59.0%	104	47.9%	103	47.5%
9	402	03/21/2018	21,141	20,061	1,080	844	378	291	77.0%	253	66.9%	251	66.4%
10	608	03/21/2018	10,319	9,795	524	377	184	113	61.4%	88	47.8%	87	47.3%
11	405	05/02/2018	11,133	10,367	766	615	269	261	97.0%	204	75.8%	204	75.8%
12	437	05/02/2018	15,143	14,537	606	606	213	200	93.9%	171	80.3%	171	80.3%
13	558	05/25/2018	24,575	22,807	1,768	1,234	619	456	73.7%	387	62.5%	387	62.5%
14	657	06/02/2018	18,370	17,390	980	773	343	216	63.0%	178	51.9%	176	51.3%
15	518	06/08/2018	4,628	4,434	194	148	68	47	69.1%	35	51.5%	35	51.5%
16	573	07/10/2018	48,293	46,167	2,126	1,513	745	611	82.0%	498	66.8%	495	66.4%
17	St Cloud	/18/2018	19,002	17,953	1,049	831	367	400	109.0%	345	94.0%	343	93.5%

Adherence to intervention

- CTD 15.4% switched back to HCTZ
- HCTZ 3.8% switched to CTD
- Mean medication possession ratio in CTD 79.5% and in 79.1% in HCTZ group

DCP Conclusions

- Pragmatic trials are possible
- Need to be creative above solving problems
- Simple inclusion/exclusion criteria with streamlined recruitment process allows for rapid recruitment and consenting of participants
- Adherence to intervention without reminders/prompting doesn't seem to be a problem