

Supplemental Materials

Supplemental Table 1. Risk factor definitions and diagnosis codes

Eligibility Criteria:

- Office visit (see definitions below) between 1/1/2012 and 12/31/2016 (study dates)
- Age 25-75 at the time of encounter
- On or prior to this office visit (within 12 months) patient has one of the following pre-diabetes criteria:
 - Pre-diabetes A1C: 5.7-6.4%
 - Pre-diabetes fasting glucose (or glucose measured on same day as lipid panel): 100-125 mg/dL
- Prior to this office visit patient has at least one documented encounter (ie criteria to define enrollment in system)
- Patient has some clinical activity 3 years after the index visit
- **Exclude** any patients with type 1 or type 2 diabetes by any of the following criteria on or prior to this office visit:
 - Diabetes diagnosis: ICD-09 250.* / ICD-10 E10.* or E11.*
 - Diabetes related pharmacotherapy or procedure (ie HEDIS criteria)
 - A1C: greater than 6.4
 - Fasting glucose (or glucose measured on same day as lipid panel): greater than 125 mg/dL
 - Random glucose \geq 200 mg/dL on 2 occasions (within 3 months of each other)
 - 2 hour glucose > 199 mg/dL
- Also exclude patients with any of the following documented conditions:
 - pregnant within 24 months of index visit

Outcome definition:

- **Time to first encounter** (from index office visit) meeting type 2 diabetes by any of the following criteria:
 - Diabetes diagnosis: ICD-09 250.* / ICD-10 E10.* or E11.*
 - Diabetes related pharmacotherapy or procedure (by HEDIS criteria)
 - A1C: greater than 6.4 (requires confirmation by HEDIS criteria or additional lab)
 - Fasting glucose (or glucose measured on same day as lipid panel): greater than 125 mg/dL (requires confirmation by HEDIS criteria or additional lab)
 - 2 hour > 199 (requires confirmation by HEDIS criteria or additional lab)
- Censor follow up for patients who do not meet outcome definition on the earliest occurrence of any of the following:
 - time of death
 - last encounter or end of enrollment in system
 - initiation of diabetes medication

Office visit definitions used for OLDW cohort:

Has an office visit during study period defined as any of the following:

- Patient encounter (variable name: "INTERACTION_TYPE") categorized as "Office or clinic patient"
- Patient encounter with one of the following procedure codes:

CPT/HCPCS Codes	Description
99201–99205, 99211–99215	Evaluation & Management Office Visit
99241–99245	Evaluation & Management Office Consultation
99381–99387, 99391–99397	Evaluation & Management Preventive Visit
99401–99404	Preventative Medicine: Individual Counseling Visit
99411–99412	Preventative Medicine: Group Counseling Visit
99420, 99429	Other Preventive Medicine Services
G0402	Initial Preventive Physical Examination ("Welcome to Medicare" Visit)
G0438, G0439	Medicare Annual Wellness Visit
G0463	Hospital outpatient clinic visit for assessment and management of a patient
T1015	Clinic visit/encounter, all inclusive

Supplemental Table 2. Refit model using complete case DPP data for estimating metformin treatment benefit

	HR	Lower	Upper	z	P
Age, per 10 years	0.91	0.90	0.92	-1.67	.10
Female	1.06	0.87	1.29	0.59	.55
Black vs white	9.81	0.85	113.68	1.83	.07
Other race vs white	3.82	0.01	1362.73	0.45	.66
Current smoker vs never	1.22	0.94	1.58	1.52	.13
Former smoker vs never	0.95	0.80	1.14	-0.52	.61
HTN	1.09	0.90	1.33	0.88	.38
A1c, per 0.1%	1.09	0.88	1.35	7.98	<.001
FPG, per 10 mg/dL	1.93	1.91	1.95	12.88	<.001
Triglycerides, per 10 mg/dL	1.02	1.02	1.02	3.78	<.001
BMI, per 5 units	1.04	1.02	1.06	0.93	.36
SBP, per 20 mmHG	1.07	1.06	1.07	0.95	.34
HDL, per 10 mg/dL	0.95	0.94	0.96	-1.16	.25
Black *BMI	0.99	0.96	1.03	-0.46	.65
Black *A1c	0.70	0.49	0.99	-2.02	.04
Other race*BMI	1.02	0.95	1.09	0.49	.62
Other race*A1c	0.72	0.29	1.83	-0.69	.49
C-statistic		0.719			
Optimism corrected c-statistic		0.710			
Calibration slope (bootstrap)		0.951			
Baseline hazard at 3 years		0.2016			

Supplemental Table 3. Metformin relative risk reduction look-up table

3-year risk (usual care)	HR	RRR	3-year risk (metformin)	ARR	NNT	
1%	1.00	0.00	1.0%	0.0%	-	HR = hazard ratio
2%	1.00	0.00	2.0%	0.0%	-	RRR= relative risk reduction
3%	1.00	0.00	3.0%	0.0%	-	ARR = absolute risk reduction
4%	1.00	0.00	4.0%	0.0%	-	NNT= number needed to treat
5%	1.00	0.00	5.0%	0.0%	-	
6%	1.00	0.00	6.0%	0.0%	-	
7%	1.00	0.00	7.0%	0.0%	-	
8%	1.00	0.00	8.0%	0.0%	-	
9%	0.99	0.01	8.9%	0.1%	1558	
10%	0.96	0.04	9.6%	0.4%	241	
11%	0.92	0.08	10.1%	0.9%	110	
12%	0.89	0.11	10.7%	1.3%	79	
13%	0.86	0.14	11.2%	1.8%	57	
14%	0.84	0.16	11.8%	2.2%	45	
15%	0.82	0.18	12.3%	2.7%	37	
16%	0.80	0.20	12.8%	3.2%	31	
17%	0.78	0.22	13.2%	3.8%	27	
18%	0.76	0.24	13.6%	4.4%	23	
19%	0.74	0.26	14.1%	4.9%	21	
20%	0.73	0.27	14.6%	5.4%	19	
21%	0.71	0.29	15.0%	6.0%	17	
22%	0.70	0.30	15.4%	6.6%	16	
23%	0.69	0.31	15.9%	7.1%	14	
24%	0.68	0.32	16.3%	7.7%	13	
25%	0.67	0.33	16.7%	8.3%	12	
26%	0.65	0.35	17.0%	9.0%	12	
27%	0.65	0.35	17.5%	9.5%	11	
28%	0.64	0.36	17.9%	10.1%	10	
29%	0.63	0.37	18.2%	10.8%	10	
30%	0.62	0.38	18.5%	11.5%	9	
31%	0.61	0.39	19.0%	12.0%	9	
32%	0.60	0.40	19.3%	12.7%	8	
33%	0.60	0.40	19.7%	13.3%	8	
34%	0.59	0.41	19.9%	14.1%	8	
35%	0.58	0.42	20.4%	14.6%	7	
36%	0.57	0.43	20.6%	15.4%	7	
37%	0.57	0.43	21.0%	16.0%	7	
38%	0.56	0.44	21.4%	16.6%	7	

39%	0.55	0.45	21.6%	17.4%	6	
40%	0.55	0.45	21.9%	18.1%	6	
41%	0.54	0.46	22.3%	18.7%	6	
42%	0.53	0.47	22.5%	19.5%	6	
43%	0.53	0.47	22.8%	20.2%	5	
44%	0.53	0.47	23.1%	20.9%	5	
45%	0.52	0.48	23.5%	21.5%	5	
46%	0.51	0.49	23.6%	22.4%	5	
47%	0.51	0.49	23.9%	23.1%	5	
48%	0.50	0.50	24.2%	23.8%	5	
49%	0.50	0.50	24.5%	24.5%	5	
50%	0.50	0.50	24.8%	25.2%	4	
51%	0.49	0.51	25.1%	25.9%	4	
52%	0.48	0.52	25.2%	26.8%	4	
53%	0.48	0.52	25.4%	27.6%	4	
54%	0.48	0.52	25.7%	28.3%	4	
55%	0.47	0.53	26.0%	29.0%	4	
56%	0.47	0.53	26.2%	29.8%	4	
57%	0.46	0.54	26.5%	30.5%	4	
58%	0.46	0.54	26.7%	31.3%	4	
59%	0.46	0.54	26.9%	32.1%	4	Optum cohort 90th percentile of risk (59%)
60%	0.45	0.55	27.0%	33.0%	4	
61%	0.45	0.55	27.2%	33.8%	3	
62%	0.44	0.56	27.4%	34.6%	3	
63%	0.44	0.56	27.6%	35.4%	3	
64%	0.43	0.57	27.8%	36.2%	3	
65%	0.43	0.57	28.0%	37.0%	3	
66%	0.43	0.57	28.2%	37.8%	3	
67%	0.42	0.58	28.4%	38.6%	3	
68%	0.42	0.58	28.6%	39.4%	3	
69%	0.42	0.58	28.8%	40.2%	3	
70%	0.41	0.59	29.0%	41.0%	3	
71%	0.41	0.59	28.9%	42.1%	3	Optum cohort 95th percentile of risk (71%)
72%	0.40	0.60	29.1%	42.9%	3	
73%	0.40	0.60	29.2%	43.8%	3	RRR truncated at 60%
74%	0.40	0.60	29.6%	44.4%	3	
75%	0.40	0.60	30.0%	45.0%	3	
76%	0.40	0.60	30.4%	45.6%	3	
77%	0.40	0.60	30.8%	46.2%	3	
78%	0.40	0.60	31.2%	46.8%	3	
79%	0.40	0.60	31.6%	47.4%	3	
80%	0.40	0.60	32.0%	48.0%	3	

81%	0.40	0.60	32.4%	48.6%	3	
82%	0.40	0.60	32.8%	49.2%	3	
83%	0.40	0.60	33.2%	49.8%	3	
84%	0.40	0.60	33.6%	50.4%	2	
85%	0.40	0.60	34.0%	51.0%	2	
86%	0.40	0.60	34.4%	51.6%	2	
87%	0.40	0.60	34.8%	52.2%	2	
88%	0.40	0.60	35.2%	52.8%	2	
89%	0.40	0.60	35.6%	53.4%	2	
90%	0.40	0.60	36.0%	54.0%	2	
91%	0.40	0.60	36.4%	54.6%	2	
92%	0.40	0.60	36.8%	55.2%	2	
93%	0.40	0.60	37.2%	55.8%	2	
94%	0.40	0.60	37.6%	56.4%	2	
95%	0.40	0.60	38.0%	57.0%	2	
96%	0.40	0.60	38.4%	57.6%	2	
97%	0.40	0.60	38.8%	58.2%	2	
98%	0.40	0.60	39.2%	58.8%	2	
99%	0.40	0.60	39.6%	59.4%	2	
100%	0.40	0.60	40.0%	60.0%	2	