

# UNSW CRAIC: Prevalent new-user cohort design

Malcolm Gillies

<https://github.com/mbg-unsw/pnuc>

5 February 2024

main@02a7e1e 2024-02-02

# Talk outline

- What & why
- Literature review
- In context
- Step by step
- Example
- Developments

# Why *prevalent* new-user?

- *i.e.* Compare those staying on old tx with switchers to new
- Increase sample size if few treatment-naïve patients
- Better external validity if disease progression
- Key feature: conditioning on length of exposure
- Alternative to Marginal Structure Models (MSM)

# Popularity of the PNUC design

- Lit review of PNUC to 9 May 2022
- 19 publications found
- 80% were collaborations with McGill
- Noone has published code

Tazare et al. (2022)

main@02a7e1e 2024-02-02

# Active comparator new-user (ACNU) cohort design

- Problems avoided by the ACNU design:
  - Confounding by indication (inactive comparator)
  - Healthy adherer bias (prevalent users)

# PNUC design in context

Increasingly restrictive ↓	<b>No-use</b>	<b>Traditional no use</b> <b>No use episodes</b>
	<b>Active-comparator</b>	<b>Generalized prevalent new user</b> <b>Prevalent new user</b> <b>Hierarchical prevalent new user</b> <b>Active comparator new user</b>

Wintzell et al. (2022)

main@02a7e1e 2024-02-02

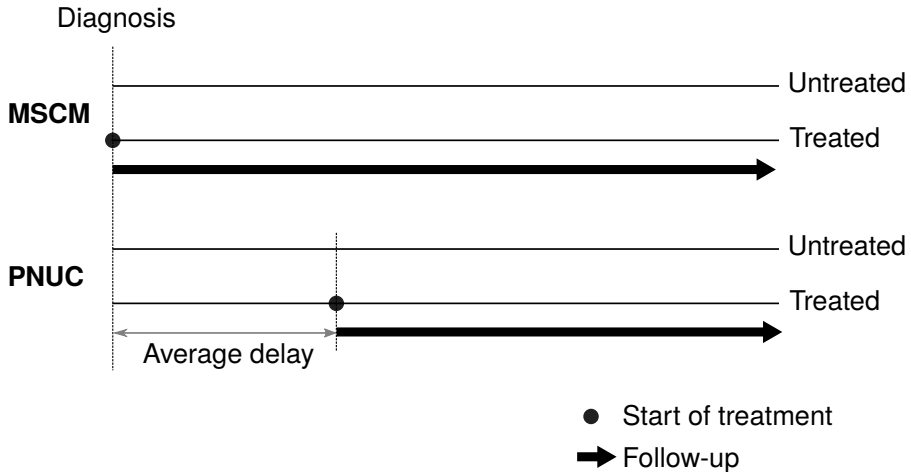
# PNUC vs MSM

	PNUC	MSM
Complexity	Higher	Lower
Computation	Higher	Lower
Precision	Higher?	Lower?

Webster-Clark et al. (2022)

main@02a7e1e 2024-02-02

# Estimands





# Prevalent new-user cohort design step by step

- 1 Defining the base cohort
- 2 Forming exposure sets
- 3 Estimating the propensity score
- 4 Matching and forming the analysis cohort
- 5 Estimating the causal effect

# Defining exposure sets and estimating the propensity score

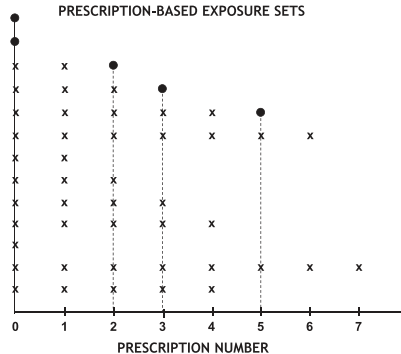


Figure 3. Depiction of a base cohort formed of 13 subjects with prescription-based exposure sets defined by the number of comparator drug prescriptions (x) before the first study drug prescription (•) was given

Suissa et al. (2017)

# Time-conditional propensity score

- Measured at treatment time
- Positivity verified within exposure set
- Score from conditional logistic regression or Cox
- Prevalent users can fall into multiple exposure sets

# Matching

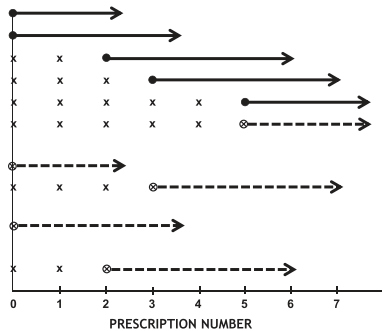


Figure 4. Depiction of the final prevalent new-user comparative cohort with comparator drug subjects matched to study drug subjects on the number of comparator drug prescriptions (x) before the first study drug prescription (●) was given, with the arrows indicating the follow-up period for outcomes

# Informative censoring among comparator group

- Follow-up of comparator group is censored if study treatment starts
- Starting treatment = patient is still alive (but sicker?)
- Remove bias through inverse probability of censoring weights (IPCW)

# Example study

1991, 1992, 1993  
1994, 1995, 1996  
1997, 1998, 1999  
2000, 2001, 2002  
2003, 2004, 2005  
2006, 2007, 2008  
2009, 2010, 2011  
2012, 2013, 2014  
2015, 2016, 2017  
2018, 2019, 2020  
2021, 2022, 2023  
2024, 2025, 2026  
2027, 2028, 2029  
2030, 2031, 2032  
2033, 2034, 2035  
2036, 2037, 2038  
2039, 2040, 2041  
2042, 2043, 2044  
2045, 2046, 2047  
2048, 2049, 2050  
2051, 2052, 2053  
2054, 2055, 2056  
2057, 2058, 2059  
2060, 2061, 2062  
2063, 2064, 2065  
2066, 2067, 2068  
2069, 2070, 2071  
2072, 2073, 2074  
2075, 2076, 2077  
2078, 2079, 2080  
2081, 2082, 2083  
2084, 2085, 2086  
2087, 2088, 2089  
2090, 2091, 2092  
2093, 2094, 2095  
2096, 2097, 2098  
2099, 2100, 2101  
2102, 2103, 2104  
2105, 2106, 2107  
2108, 2109, 2110  
2111, 2112, 2113  
2114, 2115, 2116  
2117, 2118, 2119  
2120, 2121, 2122  
2123, 2124, 2125  
2126, 2127, 2128  
2129, 2130, 2131  
2132, 2133, 2134  
2135, 2136, 2137  
2138, 2139, 2140  
2141, 2142, 2143  
2144, 2145, 2146  
2147, 2148, 2149  
2150, 2151, 2152  
2153, 2154, 2155  
2156, 2157, 2158  
2159, 2160, 2161  
2162, 2163, 2164  
2165, 2166, 2167  
2168, 2169, 2170  
2171, 2172, 2173  
2174, 2175, 2176  
2177, 2178, 2179  
2180, 2181, 2182  
2183, 2184, 2185  
2186, 2187, 2188  
2189, 2190, 2191  
2192, 2193, 2194  
2195, 2196, 2197  
2198, 2199, 2200  
2201, 2202, 2203  
2204, 2205, 2206  
2207, 2208, 2209  
2210, 2211, 2212  
2213, 2214, 2215  
2216, 2217, 2218  
2219, 2220, 2221  
2222, 2223, 2224  
2225, 2226, 2227  
2228, 2229, 2230  
2231, 2232, 2233  
2234, 2235, 2236  
2237, 2238, 2239  
2240, 2241, 2242  
2243, 2244, 2245  
2246, 2247, 2248  
2249, 2250, 2251  
2252, 2253, 2254  
2255, 2256, 2257  
2258, 2259, 2260  
2261, 2262, 2263  
2264, 2265, 2266  
2267, 2268, 2269  
2270, 2271, 2272  
2273, 2274, 2275  
2276, 2277, 2278  
2279, 2280, 2281  
2282, 2283, 2284  
2285, 2286, 2287  
2288, 2289, 2290  
2291, 2292, 2293  
2294, 2295, 2296  
2297, 2298, 2299  
2300, 2301, 2302  
2303, 2304, 2305  
2306, 2307, 2308  
2309, 2310, 2311  
2312, 2313, 2314  
2315, 2316, 2317  
2318, 2319, 2320  
2321, 2322, 2323  
2324, 2325, 2326  
2327, 2328, 2329  
2330, 2331, 2332  
2333, 2334, 2335  
2336, 2337, 2338  
2339, 2340, 2341  
2342, 2343, 2344  
2345, 2346, 2347  
2348, 2349, 2350  
2351, 2352, 2353  
2354, 2355, 2356  
2357, 2358, 2359  
2360, 2361, 2362  
2363, 2364, 2365  
2366, 2367, 2368  
2369, 2370, 2371  
2372, 2373, 2374  
2375, 2376, 2377  
2378, 2379, 2380  
2381, 2382, 2383  
2384, 2385, 2386  
2387, 2388, 2389  
2390, 2391, 2392  
2393, 2394, 2395  
2396, 2397, 2398  
2399, 2400, 2401  
2402, 2403, 2404  
2405, 2406, 2407  
2408, 2409, 2410  
2411, 2412, 2413  
2414, 2415, 2416  
2417, 2418, 2419  
2420, 2421, 2422  
2423, 2424, 2425  
2426, 2427, 2428  
2429, 2430, 2431  
2432, 2433, 2434  
2435, 2436, 2437  
2438, 2439, 2440  
2441, 2442, 2443  
2444, 2445, 2446  
2447, 2448, 2449  
2450, 2451, 2452  
2453, 2454, 2455  
2456, 2457, 2458  
2459, 2460, 2461  
2462, 2463, 2464  
2465, 2466, 2467  
2468, 2469, 2470  
2471, 2472, 2473  
2474, 2475, 2476  
2477, 2478, 2479  
2480, 2481, 2482  
2483, 2484, 2485  
2486, 2487, 2488  
2489, 2490, 2491  
2492, 2493, 2494  
2495, 2496, 2497  
2498, 2499, 2500  
2501, 2502, 2503  
2504, 2505, 2506  
2507, 2508, 2509  
2510, 2511, 2512  
2513, 2514, 2515  
2516, 2517, 2518  
2519, 2520, 2521  
2522, 2523, 2524  
2525, 2526, 2527  
2528, 2529, 2530  
2531, 2532, 2533  
2534, 2535, 2536  
2537, 2538, 2539  
2540, 2541, 2542  
2543, 2544, 2545  
2546, 2547, 2548  
2549, 2550, 2551  
2552, 2553, 2554  
2555, 2556, 2557  
2558, 2559, 2560  
2561, 2562, 2563  
2564, 2565, 2566  
2567, 2568, 2569  
2570, 2571, 2572  
2573, 2574, 2575  
2576, 2577, 2578  
2579, 2580, 2581  
2582, 2583, 2584  
2585, 2586, 2587  
2588, 2589, 2590  
2591, 2592, 2593  
2594, 2595, 2596  
2597, 2598, 2599  
2600, 2601, 2602  
2603, 2604, 2605  
2606, 2607, 2608  
2609, 2610, 2611  
2612, 2613, 2614  
2615, 2616, 2617  
2618, 2619, 2620  
2621, 2622, 2623  
2624, 2625, 2626  
2627, 2628, 2629  
2630, 2631, 2632  
2633, 2634, 2635  
2636, 2637, 2638  
2639, 2640, 2641  
2642, 2643, 2644  
2645, 2646, 2647  
2648, 2649, 2650  
2651, 2652, 2653  
2654, 2655, 2656  
2657, 2658, 2659  
2660, 2661, 2662  
2663, 2664, 2665  
2666, 2667, 2668  
2669, 2670, 2671  
2672, 2673, 2674  
2675, 2676, 2677  
2678, 2679, 2680  
2681, 2682, 2683  
2684, 2685, 2686  
2687, 2688, 2689  
2690, 2691, 2692  
2693, 2694, 2695  
2696, 2697, 2698  
2699, 2700, 2701  
2702, 2703, 2704  
2705, 2706, 2707  
2708, 2709, 2710  
2711, 2712, 2713  
2714, 2715, 2716  
2717, 2718, 2719  
2720, 2721, 2722  
2723, 2724, 2725  
2726, 2727, 2728  
2729, 2730, 2731  
2732, 2733, 2734  
2735, 2736, 2737  
2738, 2739, 2740  
2741, 2742, 2743  
2744, 2745, 2746  
2747, 2748, 2749  
2750, 2751, 2752  
2753, 2754, 2755  
2756, 2757, 2758  
2759, 2760, 2761  
2762, 2763, 2764  
2765, 2766, 2767  
2768, 2769, 2770  
2771, 2772, 2773  
2774, 2775, 2776  
2777, 2778, 2779  
2780, 2781, 2782  
2783, 2784, 2785  
2786, 2787, 2788  
2789, 2790, 2791  
2792, 2793, 2794  
2795, 2796, 2797  
2798, 2799, 2800  
2801, 2802, 2803  
2804, 2805, 2806  
2807, 2808, 2809  
2810, 2811, 2812  
2813, 2814, 2815  
2816, 2817, 2818  
2819, 2820, 2821  
2822, 2823, 2824  
2825, 2826, 2827  
2828, 2829, 2830  
2831, 2832, 2833  
2834, 2835, 2836  
2837, 2838, 2839  
2840, 2841, 2842  
2843, 2844, 2845  
2846, 2847, 2848  
2849, 2850, 2851  
2852, 2853, 2854  
2855, 2856, 2857  
2858, 2859, 2860  
2861, 2862, 2863  
2864, 2865, 2866  
2867, 2868, 2869  
2870, 2871, 2872  
2873, 2874, 2875  
2876, 2877, 2878  
2879, 2880, 2881  
2882, 2883, 2884  
2885, 2886, 2887  
2888, 2889, 2890  
2891, 2892, 2893  
2894, 2895, 2896  
2897, 2898, 2899  
2900, 2901, 2902  
2903, 2904, 2905  
2906, 2907, 2908  
2909, 2910, 2911  
2912, 2913, 2914  
2915, 2916, 2917  
2918, 2919, 2920  
2921, 2922, 2923  
2924, 2925, 2926  
2927, 2928, 2929  
2930, 2931, 2932  
2933, 2934, 2935  
2936, 2937, 2938  
2939, 2940, 2941  
2942, 2943, 2944  
2945, 2946, 2947  
2948, 2949, 2950  
2951, 2952, 2953  
2954, 2955, 2956  
2957, 2958, 2959  
2960, 2961, 2962  
2963, 2964, 2965  
2966, 2967, 2968  
2969, 2970, 2971  
2972, 2973, 2974  
2975, 2976, 2977  
2978, 2979, 2980  
2981, 2982, 2983  
2984, 2985, 2986  
2987, 2988, 2989  
2990, 2991, 2992  
2993, 2994, 2995  
2996, 2997, 2998  
2999, 3000, 3001  
3002, 3003, 3004  
3005, 3006, 3007  
3008, 3009, 3010  
3011, 3012, 3013  
3014, 3015, 3016  
3017, 3018, 3019  
3020, 3021, 3022  
3023, 3024, 3025  
3026, 3027, 3028  
3029, 3030, 3031  
3032, 3033, 3034  
3035, 3036, 3037  
3038, 3039, 3040  
3041, 3042, 3043  
3044, 3045, 3046  
3047, 3048, 3049  
3050, 3051, 3052  
3053, 3054, 3055  
3056, 3057, 3058  
3059, 3060, 3061  
3062, 3063, 3064  
3065, 3066, 3067  
3068, 3069, 3070  
3071, 3072, 3073  
3074, 3075, 3076  
3077, 3078, 3079  
3080, 3081, 3082  
3083, 3084, 3085  
3086, 3087, 3088  
3089, 3090, 3091  
3092, 3093, 3094  
3095, 3096, 3097  
3098, 3099, 3100  
3101, 3102, 3103  
3104, 3105, 3106  
3107, 3108, 3109  
3110, 3111, 3112  
3113, 3114, 3115  
3116, 3117, 3118  
3119, 3120, 3121  
3122, 3123, 3124  
3125, 3126, 3127  
3128, 3129, 3130  
3131, 3132, 3133  
3134, 3135, 3136  
3137, 3138, 3139  
3140, 3141, 3142  
3143, 3144, 3145  
3146, 3147, 3148  
3149, 3150, 3151  
3152, 3153, 3154  
3155, 3156, 3157  
3158, 3159, 3160  
3161, 3162, 3163  
3164, 3165, 3166  
3167, 3168, 3169  
3170, 3171, 3172  
3173, 3174, 3175  
3176, 3177, 3178  
3179, 3180, 3181  
3182, 3183, 3184  
3185, 3186, 3187  
3188, 3189, 3190  
3191, 3192, 3193  
3194, 3195, 3196  
3197, 3198, 3199  
3200, 3201, 3202  
3203, 3204, 3205  
3206, 3207, 3208  
3209, 3210, 3211  
3212, 3213, 3214  
3215, 3216, 3217  
3218, 3219, 3220  
3221, 3222, 3223  
3224, 3225, 3226  
3227, 3228, 3229  
3230, 3231, 3232  
3233, 3234, 3235  
3236, 3237, 3238  
3239, 3240, 3241  
3242, 3243, 3244  
3245, 3246, 3247  
3248, 3249, 3250  
3251, 3252, 3253  
3254, 3255, 3256  
3257, 3258, 3259  
3260, 3261, 3262  
3263, 3264, 3265  
3266, 3267, 3268  
3269, 3270, 3271  
3272, 3273, 3274  
3275, 3276, 3277  
3278, 3279, 3280  
3281, 3282, 3283  
3284, 3285, 3286  
3287, 3288, 3289  
3290, 3291, 3292  
3293, 3294, 3295  
3296, 3297, 3298  
3299, 3300, 3301  
3302, 3303, 3304  
3305, 3306, 3307  
3308, 3309, 3310  
3311, 3312, 3313  
3314, 3315, 3316  
3317, 3318, 3319  
3320, 3321, 3322  
3323, 3324, 3325  
3326, 3327, 3328  
3329, 3330, 3331  
3332, 3333, 3334  
3335, 3336, 3337  
3338, 3339, 3340  
3341, 3342, 3343  
3344, 3345, 3346  
3347, 3348, 3349  
3350, 3351, 3352  
3353, 3354, 3355  
3356, 3357, 3358  
3359, 3360, 3361  
3362, 3363, 3364  
3365, 3366, 3367  
3368, 3369, 3370  
3371, 3372, 3373  
3374, 3375, 3376  
3377, 3378, 3379  
3380, 3381, 3382  
3383, 3384, 3385  
3386, 3387, 3388  
3389, 3390, 3391  
3392, 3393, 3394  
3395, 3396, 3397  
3398, 3399, 3400  
3401, 3402, 3403  
3404, 3405, 3406  
3407, 3408, 3409  
3410, 3411, 3412  
3413, 3414, 3415  
3416, 3417, 3418  
3419, 3420, 3421  
3422, 3423, 3424  
3425, 3426, 3427  
3428, 3429, 3430  
3431, 3432, 3433  
3434, 3435, 3436  
3437, 3438, 3439  
3440, 3441, 3442  
3443, 3444, 3445  
3446, 3447, 3448  
3449, 3450, 3451  
3452, 3453, 3454  
3455, 3456, 3457  
3458, 3459, 3460  
3461, 3462, 3463  
3464, 3465, 3466  
3467, 3468, 3469  
3470, 3471, 3472  
3473, 3474, 3475  
3476, 3477, 3478  
3479, 3480, 3481  
3482, 3483, 3484  
3485, 3486, 3487  
3488, 3489, 3490  
3491, 3492, 3493  
3494, 3495, 3496  
3497, 3498, 3499  
3500, 3501, 3502  
3503, 3504, 3505  
3506, 3507, 3508  
3509, 3510, 3511  
3512, 3513, 3514  
3515, 3516, 3517  
3518, 3519, 3520  
3521, 3522, 3523  
3524, 3525, 3526  
3527, 3528, 3529  
3530, 3531, 3532  
3533, 3534, 3535  
3536, 3537, 3538  
3539, 3540, 3541  
3542, 3543, 3544  
3545, 3546, 3547  
3548, 3549, 3550  
3551, 3552, 3553  
3554, 3555, 3556  
3557, 3558, 3559  
3560, 3561, 3562  
3563, 3564, 3565  
3566, 3567, 3568  
3569, 3570, 3571  
3572, 3573, 3574  
3575, 3576, 3577  
3578, 3579, 3580  
3581, 3582, 3583  
3584, 3585, 3586  
3587, 3588, 3589  
3590, 3591, 3592  
3593, 3594, 3595  
3596, 3597, 3598  
3599, 3600, 3601  
3602, 3603, 3604  
3605, 3606, 3607  
3608, 3609, 3610  
3611, 3612, 3613  
3614, 3615, 3616  
3617, 3618, 3619  
3620, 3621, 3622  
3623, 3624, 3625  
3626, 3627, 3628  
3629, 3630, 3631  
3632, 3633, 3634  
3635, 3636, 3637  
3638, 3639, 3640  
3641, 3642, 3643  
3644, 3645, 3646  
3647, 3648, 3649  
3650, 3651, 3652  
3653, 3654, 3655  
3656, 3657, 3658  
3659, 3660, 3661  
3662, 3663, 3664  
3665, 3666, 3667  
3668, 3669, 3670  
3671, 3672, 3673  
3674, 3675, 3676  
3677, 3678, 3679  
3680, 3681, 3682  
3683, 3684, 3685  
3686, 3687, 3688  
3689, 3690, 3691  
3692, 3693, 3694  
3695, 3696, 3697  
3698, 3699, 3700  
3701, 3702, 3703  
3704, 3705, 3706  
3707, 3708, 3709  
3710, 3711, 3712  
3713, 3714, 3715  
3716, 3717, 3718  
3719, 3720, 3721  
3722, 3723, 3724  
3725, 3726, 3727  
3728, 3729, 3730  
3731, 3732, 3733  
3734, 3735, 3736  
3737, 3738, 3739  
3740, 3741, 3742  
3743, 3744, 3745  
3746, 3747, 3748  
3749, 3750, 3751  
3752, 3753, 3754  
3755, 3756, 3757  
3758, 3759, 3760  
3761, 3762, 3763  
3764, 3765, 3766  
3767, 3768, 3769  
3770, 3771, 3772  
3773, 3774, 3775  
3776, 3777, 3778  
3779, 3780, 3781  
3782, 3783, 3784  
3785, 3786, 3787  
3788, 3789, 3790  
3791, 3792, 3793  
3794, 3795, 3796  
3797, 3798, 3799  
3800, 3801, 3802  
3803, 3804, 3805  
3806, 3807, 3808  
3809, 3810, 3811  
3812, 3813, 3814  
3815, 3816, 3817  
3818, 3819, 3820  
3821, 3822, 3823  
3824, 3825, 3826  
3827, 3828, 3829  
3830, 3831, 3832  
3833, 3834, 3835  
3836, 3837, 3838  
3839, 3840, 3841  
3842, 3843, 3844  
3845, 3846, 3847  
3848, 3849, 3850  
3851, 3852, 3853  
3854, 3855, 3856  
3857, 3858, 3859  
3860, 3861, 3862  
3863, 3864, 3865  
3866, 3867, 3868  
3869, 3870, 3871  
3872, 3873, 3874  
3875, 3876, 3877  
3878, 3879, 3880  
3881, 3882, 3883  
3884, 3885, 3886  
3887, 3888, 3889  
3890, 3891, 3892  
3893, 3894, 3895  
3896, 3897, 3898  
3899, 3900, 3901  
3902, 3903, 3904  
3905, 3906, 3907  
3908, 3909, 3910  
3911, 3912, 3913  
3914, 3915, 3916  
3917, 3918, 3919  
3920, 3921, 3922  
3923, 3924, 3925  
3926, 3927, 3928  
3929, 3930, 3931  
3932, 3933, 3934  
3935, 3936, 3937  
3938, 3939, 3940  
3941, 3942, 3943  
3944, 3945, 3946  
3947, 3948, 3949  
3950, 3951, 3952  
3953, 3954, 3955  
3956, 3957, 3958  
3959, 3960, 3961  
3962, 3963, 3964  
3965, 3966, 3967  
3968, 3969, 3970  
3971, 3972, 3973  
3974, 3975, 3976  
3977, 3978, 3979  
3980, 3981, 3982  
3983, 3984, 3985  
3986, 3987, 3988  
3989, 3990, 3991  
3992, 3993, 3994  
3995, 3996, 3997  
3998, 3999, 4000  
4001, 4002, 4003  
4004, 4005, 4006  
4007, 4008, 4009  
4010, 4011, 4012  
4013, 4014, 4015  
4016, 4017, 4018  
4019, 4020, 4021  
4022, 4023, 4024  
4025, 4026, 4027  
4028, 4029, 4030  
4031, 4032, 4033  
4034, 4035, 4036  
4037, 4038, 4039  
4040, 4041, 4042  
4043, 4

# What is the paper about?

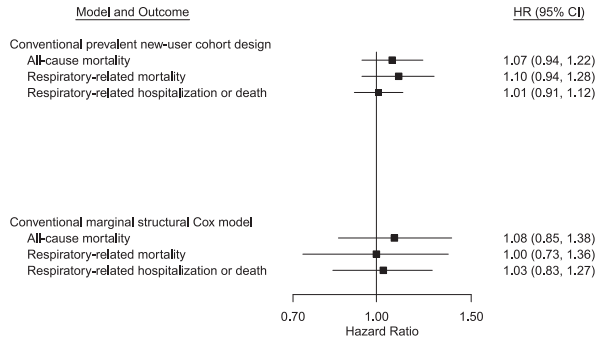
- Question: Are PPIs efficacious in idiopathic pulmonary fibrosis?
- Data: UK linked GP and hospital data (CPRD-GOLD/HES/ONS),  $n = 2944$
- Outcomes: All-cause mortality, respiratory death, hospitalisation
- Covariates: Demographics, comorbidity, medicines (all time-varying)
- Compare results from three different study designs

# Idiopathic Pulmonary Fibrosis (IPF)

- Progressive scarring of the lungs, cause unknown
- Average life expectancy after diagnosis about four years
- Pirfenidone (2008) and nintedanib (2014) slow progression
- Proton pump inhibitors also guideline recommended (weak evidence)
- Contention: PPI effects seen in earlier studies are due to bias

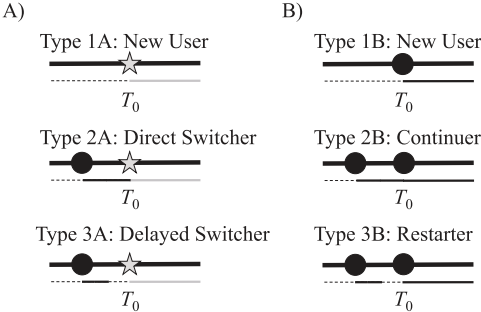


# Results



**Figure 3.** Hazard ratios (HRs) for respiratory-disease-related hospitalization and mortality associated with proton pump inhibitor use (compared with no use) obtained using 3 different study designs in a cohort of patients with idiopathic pulmonary fibrosis, United Kingdom, 2003–2016. Bars, 95% confidence intervals (CIs).

# PNUC sub-cohorts



**Figure 1.** Infographic showing treatment histories of various types of initiators of treatment A and users of B. Panel A includes the initiators of treatment A (types 1A–3A) and panel B includes the 3 corresponding individuals taking treatment B that would be “ideal” counterfactual contrasts for types 1A–3A. Gray stars represent prescriptions for A, while black circles represent prescriptions for B. Below each set of prescriptions is a secondary timeline showing time with no treatment (dashed black), time treated with A (gray), and time treated with B (solid black).

Webster-Clark et al. (2021)

# Developments

- Matching with/without replacement or weighting
- How to condition on “length of exposure”?
- Positivity and matching
- Estimating the propensity score
- Discontinuation only; intensification

Webster-Clark et al. (2022)

main@02a7e1e 2024-02-02

# Discussion

- Does the PNUC design look useful to you?
- Would you use it rather than a marginal structural model?
- What are the barriers to using these methods?

# References

- S. Suissa, E. E. M. Moodie, and S. Dell’Aniello. Prevalent new-user cohort designs for comparative drug effect studies by time-conditional propensity scores. *Pharmacoepidemiology and Drug Safety*, 26(4):459–468, 2017. doi: 10.1002/pds.4107. URL <https://onlinelibrary.wiley.com/doi/abs/10.1002/pds.4107>.
- J. Tazare, D. C. Gibbons, M. Bokern, E. J. Williamson, I. A. Gillespie, M. Cunningham, J. Logie, and I. J. Douglas. Prevalent new user designs: a literature review of current implementation practice. *Pharmacoepidemiology and Drug Safety*, 2022. doi: 10.1002/pds.5656. URL <https://onlinelibrary.wiley.com/doi/abs/10.1002/pds.5656>.
- T. Tran and S. Suissa. Comparing New-User Cohort Designs: The Example of Proton Pump Inhibitor Effectiveness in Idiopathic Pulmonary Fibrosis. *American Journal of Epidemiology*, 190(5):928–938, 2021. doi: 10.1093/aje/kwaa242. URL <https://doi.org/10.1093/aje/kwaa242>.
- M. Webster-Clark. The prevalent new user design: establishing the estimand and sources of bias, 2020. URL [https://pharmacoepi.unc.edu/wp-content/uploads/sites/6788/2020/12/Webster-Clark\\_Michael\\_PNU.pdf](https://pharmacoepi.unc.edu/wp-content/uploads/sites/6788/2020/12/Webster-Clark_Michael_PNU.pdf). Accessed: 2024-01-15.
- M. Webster-Clark, R. K. Ross, and J. L. Lund. Initiator Types and the Causal Question of the Prevalent New-User Design: A Simulation Study. *American Journal of Epidemiology*, 190(7):1341–1348, 2021. doi: 10.1093/aje/kwaa283. URL <https://academic.oup.com/aje/article/190/7/1341/6043913>.
- M. Webster-Clark, P. Mavros, E. M. Garry, T. Stürmer, S. Shmuel, J. Young, and C. Girman. Alternative analytic and matching approaches for the prevalent new-user design: A simulation study. *Pharmacoepidemiology and Drug Safety*, 31(7):796–803, 2022. doi: 10.1002/pds.5446. URL <https://onlinelibrary.wiley.com/doi/abs/10.1002/pds.5446>.
- V. Wintzell, H. Svanström, and B. Pasternak. Selection of Comparator Group in Observational Drug Safety Studies: Alternatives to the Active Comparator New User Design. *Epidemiology*, 33(5):707, 2022. doi: 10.1097/EDE.0000000000001521. URL [https://journals.lww.com/epidem/fulltext/2022/09000/selection\\_of\\_comparator\\_group\\_in\\_observational.14.aspx](https://journals.lww.com/epidem/fulltext/2022/09000/selection_of_comparator_group_in_observational.14.aspx).

# Acknowledgments

- An earlier version was presented to the Medicine Intelligence CRE methods journal club on 1 July 2021