Supplementary material file 11-103-01-suppl2: Health-economic analyses relating to Chapter 4

S2.1. Measurement model: results tables for primary analysis evaluating the ability of estimated GFR equations to identify NICE accelerated progression.

Note that in each of these tables the number of patients tested each year is equal to the total cohort minus the number of patients that have had a previous TP or delayed positive result (following a missed true progression event)

Table 1. 10-year clinical accuracy simulation results: MDRD equation, combined NICE progression criteria.

Year	% Tested[a] (out of total cohort)	% Positive (out of all tested)	% FPs (out of all positives)	% TP (out of all positives)	% Negative (out of all tested)	% FN (out of all negatives)	FN: average delay (years)	FN: % never identified (out of FNs)	Sensitivity (cumulative)	Specificity (cumulative)
Year 1	100.0% [100 – 100]	14.2% [11.6 – 17.1]	100.0% [99.7 - 100]	0.0% [0.0 – 0.3]	85.8% [82.9 – 88.4]	0.0% [0.0 – 0.2]	2.1 [1.7 – 2.5]	0.0% [0.0 – 0.0]	21.8% [7.5 – 38.5]	85.8% [82.9 – 88.4]
Year 2	100.0% [100 – 100]	17.8% [17.3 – 18.4]	94.0% [87.5 – 97.5]	6.0% [2.5 – 12.5]	82.2% [81.6 – 82.7]	1.4% [0.6 – 3.2]	1.0 [1.0 – 1.2]	0.0% [0.0 – 0.0]	47.5% [42.3 – 53.0]	84.4% [82.6 – 85.8]
Year 3	98.9% [97.8 – 99.5]	22.4% [15.8 – 27.0]	94.7% [89.1 – 97.7]	1.6% [0.0 – 4.5]	77.6% [73.0 – 84.2]	0.2% [0.0 – 0.9]	1.4 [1.2 – 1.6]	0.2% [0.0 – 0.9]	50.7% [40.6 – 61.9]	82.4% [81.2 – 83.6]
Year 4	97.8% [95.1 – 99.1]	15.8% [11.8 – 21.6]	98.9% [95.6 – 100]	0.7% [0.0 – 2.8]	84.2% [78.4 – 88.2]	0.2% [0.0 – 0.8]	1.4 [1.2 – 1.6]	1.1% [0.0 – 2.5]	50.0% [41.8 – 60.3]	82.9% [82.1 – 83.6]
Year 5	97.5% [95.1 – 98.8]	20.1% [19.0 – 22.0]	98.8% [94.0 – 100]	0.5% [0.0 – 3.6]	79.9% [78.0 – 81.0]	0.2% [0.0 –1.1]	1.6 [1.4 – 1.8]	3.8% [0.0 – 9.1]	50.1% [42.2 – 60.3]	82.3% [81.5 – 83.1]
Year 6	97.3% [95.1 – 98.7]	20.7% [19.5 – 22.7]	90.4% [86.7 – 94.8]	9.2% [5.2 – 12.1]	79.3% [77.3 – 80.5]	3.2% [1.9 – 4.1]	1.6 [1.5 – 1.7]	12.5% [8.7 – 16.8]	45.7% [41.5 –51.7]	82.0% [81.1 – 82.8]
Year 7	95.3% [93.4 – 97.5]	20.3% [19.0 – 22.5]	85.6% [82.6 – 88.6]	7.7% [5.8 – 9.6]	79.7% [77.5 – 81.0]	3.3% [2.5 – 4.1]	1.5 [1.5 – 1.6]	23.6% [20.6 – 26.9]	42.8% [39.4 – 47.1]	82.0% [80.9 – 82.7]
Year 8	92.5% [90.4 – 95.1]	19.9% [18.6 – 22.0]	90.1% [85.4 – 92.5]	1.0% [0.0 – 4.1]	80.1% [78.0 – 81.4]	0.4% [0.0 – 1.8]	1.3 [1.2 – 1.4]	38.1% [28.6 – 47.6]	42.6% [39.4 – 46.8]	81.9% [80.8 – 82.7]
Year 9	90.7% [88.1 – 92.9]	19.4% [18.1 – 21.7]	94.9% [91.4 – 96.5]	0.2% [0.0 – 1.4]	80.6% [78.3 – 81.9]	0.1% [0.0 – 0.6]	1.0 [1.0 – 1.0]	57.7% [42.7 – 71.1]	42.6% [39.4 – 46.8]	81.9% [80.6 – 82.6]
Year 10	89.8% [86.7 – 92.9]	18.9% [17.6 – 21.3]	85.4% [79.4 – 92.4]	11.8% [3.9 – 18.3]	81.1% [78.7 – 82.4]	5.1% [2.0 – 7.9]	NA	100.0% [100 – 100]	40.0% [37.1 – 43.3]	81.9% [80.5 – 82.7]

Table 2. 10-year clinical accuracy simulation results: CKD-EPI$_{creatinine}$ equation, combined NICE progression criteria.

Year	% Tested[a] (out of total cohort)	% Positive (out of all tested)	% FPs (out of all positives)	% TP (out of all positives)	% Negative (out of all tested)	% FN (out of all negatives)	FN: average delay (years)	FN: % never identified (out of FNs)	Sensitivity (cumulative)	Specificity (cumulative)
Year 1	100.0% [100 – 100]	15.7% [13.0 – 18.9]	99.9% [99.6 – 100]	0.1% [0.0 – 0.4]	84.3% [81.1 – 87.0]	0.0% [0.0 – 0.2]	1.8 [1.2 – 2.2]	0.0% [0.0 – 0.0]	34.1% [14.6 – 50.0]	84.3% [81.1 – 87.0]
Year 2	100.0% [99.9 – 100]	18.2% [17.5 – 18.9]	93.9% [87.4 – 97.4]	6.1% [2.6 – 12.6]	81.8% [81.1 – 82.5]	1.4% [0.5 – 3.2]	1.0 [1.0 – 1.2]	0.0% [0.0 – 0.2]	49.0% [43.4 – 54.7]	83.4% [81.4 – 85.1]
Year 3	98.9% [97.8 – 99.5]	23.2% [16.2 – 27.6]	95.0% [89.4 – 97.8]	1.5% [0.0 – 4.2]	76.8% [72.4 – 83.8]	0.2% [0.0 – 0.9]	1.4 [1.2 – 1.6]	0.1% [0.0 – 0.9]	51.8% [42.7 – 62.7]	81.5% [80.3 – 82.7]
Year 4	97.7% [95.1 – 99.0]	15.6% [11.7 – 21.4]	98.8% [95.4 – 100]	0.8% [0.0 – 2.8]	84.4% [78.6 – 88.3]	0.2% [0.0 – 0.8]	1.3 [1.2 – 1.6]	0.3% [0.0 – 2.5]	51.1% [43.0 – 61.3]	82.3% [81.5 – 83.1]
Year 5	97.5% [95.1 – 98.8]	20.2% [19.2 – 22.2]	98.8% [94.1 – 100]	0.5% [0.0 – 3.6]	79.8% [77.8 – 80.8]	0.2% [0.0 – 1.1]	1.6 [1.4 – 1.9]	3.7% [0.0 – 8.2]	51.1% [43.2 – 61.3]	81.8% [80.9 – 82.7]
Year 6	97.3% [95.1 – 98.7]	20.8% [19.7 – 22.8]	90.5% [86.9 – 94.8]	9.1% [5.1 – 12.0]	79.2% [77.2 – 80.3]	3.2% [1.9 – 4.1]	1.6 [1.5 – 1.8]	12.7% [8.6 – 16.8]	46.0% [41.8 – 52.2]	81.6% [80.6 – 82.4]
Year 7	95.3% [93.4 – 97.5]	20.4% [19.2 – 22.6]	85.7% [82.7 – 88.8]	7.6% [5.8 – 9.6]	79.6% [77.4 – 80.8]	3.3% [2.5 – 4.1]	1.5 [1.5 – 1.6]	23.7% [20.5 – 27.0]	43.0% [39.5 – 47.3]	81.6% [80.5 – 82.4]
Year 8	92.6% [90.4 – 95.1]	20.0% [18.7 – 22.1]	90.1% [85.6 – 92.6]	1.0% [0.0 – 4.1]	80.0% [77.9 – 81.3]	0.4% [0.0 – 1.8]	1.3 [1.2 – 1.4]	37.1% [28.0 – 46.1]	42.8% [39.5 – 47.1]	81.6% [80.4 – 82.4]
Year 9	90.7% [88.1 – 93.6]	19.6% [18.3 – 22.8]	94.8% [91.4 – 96.5]	0.2% [0.0 – 1.4]	80.4% [78.2 – 81.7]	0.1% [0.0 – 0.6]	1.0 [1.0 – 1.0]	55.4% [38.3 – 69.3]	42.7% [39.5 – 47.1]	81.5% [80.3 – 82.3]
Year 10	89.8% [86.7 – 92.9]	19.1% [17.9 – 21.4]	85.2% [79.1 – 92.2]	12.0% [4.0 – 18.5]	80.9% [78.6 – 82.1]	5.1% [2.0 – 7.8]	NA	100.0% [100 – 100]	40.4% [37.6 – 43.6]	81.6% [80.2 – 82.4]

Table 3. 10-year clinical accuracy simulation results: CKD-EPI$_{cystatin}$ equation, combined NICE progression criteria.

Year	% Tested[a] (out of total cohort)	% Positive (out of all tested)	% FPs (out of all positives)	% TP (out of all positives)	% Negative (out of all tested)	% FN (out of all negatives)	FN: average delay (years)	FN: % never identified (out of FNs)	Sensitivity (cumulative)	Specificity (cumulative)
Year 1	100.0% [100 – 100]	20.0% [17.6 – 22.5]	99.9% [99.0 –100]	0.1% [0.0 – 1.0]	80.0% [77.5 – 82.4]	0.0% [0.0 – 0.0]	1.0 [1.0 – 1.0]	0.0% [0.0 – 0.0]	98.3% [95.8 – 100]	80.0% [77.6 – 82.5]
Year 2	100.0% [99.8 – 100]	23.1% [22.4 – 24.4]	96.3% [92.4 – 98.6]	3.7% [1.4 – 7.6]	76.9% [75.6 – 77.7]	1.8% [0.6 – 4.1]	1.1 [1.0 – 1.2]	0.1% [0.0 – 0.4]	40.3% [33.7 – 54.3]	78.6% [77.3 – 80.1]
Year 3	99.1% [98.2 – 99.5]	25.8% [21.9 – 32.0]	94.6% [88.3 – 97.6]	1.6% [0.0 – 4.4]	74.2% [68.0 – 78.1]	0.2% [0.0 – 0.9]	1.4 [1.2 – 1.6]	0.2% [0.0 – 0.7]	45.7% [34.0 – 57.6]	77.5% [76.3 – 78.8]
Year 4	97.8% [95.2 – 98.9]	24.0% [20.6 – 27.3]	99.1% [96.6 – 100]	0.5% [0.0 – 2.0]	76.0% [72.7 – 79.4]	0.3% [0.0 – 0.9]	1.4 [1.2 – 1.8]	1.6% [0.0 – 4.0]	44.7% [33.3 – 55.8]	77.2% [76.4 – 78.2]
Year 5	97.5% [95.2 – 98.8]	22.2% [21.1 – 24.1]	98.9% [94.8 – 100]	0.4% [0.0 – 3.2]	77.8% [75.9 – 78.9]	0.2% [0.0 – 1.2]	1.7 [1.5 – 2.1]	4.6% [0.0 – 10.1]	44.6% [33.3 – 55.5]	77.3% [76.6 – 78.0]
Year 6	97.3% [95.2 – 98.8]	22.4% [21.3 – 24.2]	91.6% [88.3 – 95.5]	8.0% [4.4 – 10.7]	77.6% [75.7 – 78.7]	3.4% [2.0 – 4.3]	1.8 [1.7 – 1.9]	14.7% [11.3 – 18.4]	42.2% [36.0 – 48.7]	77.5% [76.8 – 77.9]
Year 7	95.4% [93.5 – 97.5]	21.9% [20.7 – 24.0]	87.6% [85.1 – 90.3]	6.6% [5.1 – 8.4]	78.1% [76.0 – 78.3]	3.5% [2.7 – 4.3]	1.6 [1.5 – 1.7]	28.2% [24.6 – 31.6]	39.8% [35.2 – 45.0]	77.8% [77.0 – 78.2]
Year 8	92.9% [90.8 – 95.3]	21.5% [20.3 – 23.4]	91.3% [87.3 – 93.5]	0.8% [0.0 – 3.6]	78.5% [76.6 – 79.7]	0.4% [0.0 – 1.9]	1.3 [1.3 – 1.5]	41.1% [31.1 – 48.6]	39.5% [35.2 – 44.6]	78.1% [77.2 – 78.5]
Year 9	91.1% [88.6 – 93.9]	21.1% [19.9 – 23.1]	94.9% [91.8 – 96.5]	0.2% [0.0 – 1.3]	78.9% [76.9 – 80.1]	0.1% [0.0 – 0.6]	1.0 [1.0 – 1.0]	60.2% [46.6 – 75.0]	39.5% [35.2 – 44.5]	78.3% [77.3 – 78.7]
Year 10	90.1% [87.2 – 93.2]	20.5% [19.3 – 22.6]	86.1% [80.7 – 92.4]	10.7% [3.6 – 16.5]	79.5% [77.4 – 80.7]	5.3% [2.0 – 8.1]	NA	100.0% [100 – 100]	37.9% [34.5 – 41.8]	78.5% [77.5 – 79.0]

Table 4. 10-year clinical accuracy simulation results: CKD-EPI$_{cystatin-creatinine}$ equation, combined NICE progression criteria.

Year	% Tested[a] (out of total cohort)	% Positive (out of all tested)	% FPs (out of all positives)	% TP (out of all positives)	% Negative (out of all tested)	% FN (out of all negatives)	FN: average delay (years)	FN: % never identified (out of FNs)	Sensitivity (cumulative)	Specificity (cumulative)
Year 1	100.0% [100 – 100]	14.4% [11.9 – 16.7]	99.8% [98.7 – 100]	0.2% [0.0 – 1.3]	85.6% [83.3 – 88.1]	0.0% [0.0 – 0.0]	1.0 [1.0 – 1.3]	0.0% [0.0 – 0.0]	90.9% [81.0 – 100]	85.6% [83.3 – 88.1]
Year 2	100.0% [99.8 – 100]	16.3% [15.6 – 17.4]	94.3% [88.4 – 97.7]	5.7% [2.3 – 11.6]	83.7% [82.6 – 84.4]	1.6% [0.5 – 3.6]	1.0 [1.0 – 1.1]	0.0% [0.0 – 0.4]	43.1% [35.7 – 56.7]	84.9% [83.6 – 86.5]
Year 3	99.1% [98.1 – 99.5]	22.4% [15.3 – 29.9]	94.0% [87.7 – 97.3]	1.9% [0.0 – 5.1]	77.6% [70.1 – 84.7]	0.1% [0.0 – 0.9]	1.3 [1.1 – 1.4]	0.3% [0.0 – 1.3]	47.4% [35.8 – 59.6]	82.8% [81.1 – 85.0]
Year 4	97.7% [95.1 – 99.0]	15.7% [12.1 – 20.8]	98.8% [95.1 – 100]	0.7% [0.0 – 2.6]	84.3% [79.2 – 87.9]	0.2% [0.0 – 0.8]	1.4 [1.2 – 1.9]	3.5% [0.0 – 8.3]	46.4% [35.6 – 57.8]	83.2% [82.6 – 84.2]
Year 5	97.5% [95.1 – 98.7]	17.2% [16.1 – 19.1]	98.7% [93.5 – 100]	0.6% [0.0 – 4.1]	82.8% [80.9 – 83.9]	0.1% [0.0 – 1.1]	1.8 [1.5 – 2.1]	7.8% [0.0 – 14.9]	46.3% [35.6 – 57.7]	83.2% [82.6 – 83.9]
Year 6	97.3% [95.1 – 98.7]	17.7% [16.5 – 19.8]	89.2% [85.1 – 94.3]	10.4% [5.7 – 13.8]	82.3% [80.2 – 83.5]	3.1% [1.9 – 4.0]	1.8 [1.6 – 1.9]	23.0% [17.2 – 28.9]	43.3% [37.3 – 50.4]	83.2% [82.7 – 83.7]
Year 7	95.4% [93.4 – 97.5]	16.9% [15.6 – 19.2]	84.6% [81.4 – 88.0]	8.5% [6.3 – 10.8]	83.1% [80.8 – 84.4]	3.3% [2.5 – 4.1]	1.6 [1.5 – 1.6]	39.3% [35.5 – 43.0]	40.3% [35.7 – 45.7]	83.5% [82.8 – 83.9]
Year 8	92.9% [90.8 – 95.4]	16.4% [15.1 – 18.6]	90.1% [85.2 – 92.6]	1.0% [0.0 – 4.5]	83.6% [81.4 – 84.9]	0.4% [0.0 – 1.8]	1.3 [1.2 – 1.4]	52.0% [42.9 – 60.7]	40.0% [35.7 – 45.4]	83.6% [82.9 – 84.1]
Year 9	91.4% [88.9 – 94.2]	16.1% [14.9 – 18.3]	94.5% [91.0 – 96.2]	0.3% [0.0 – 1.6]	83.9% [81.7 – 85.1]	0.1% [0.0 – 0.6]	1.0 [1.0 – 1.0]	65.6% [50.0 – 78.3]	39.9% [35.7 – 45.2]	83.7% [82.9 – 84.3]
Year 10	90.6% [87.7 – 93.6]	15.6% [14.4 – 17.9]	83.2% [76.4 – 91.3]	13.1% [4.3 – 20.3]	84.4% [82.1 – 85.6]	5.1% [1.9 – 7.8]	NA	100.0% [100 – 100]	37.5% [33.9 – 41.9]	84.0% [82.9 – 84.5]

S2.2. Measurement model: results of secondary analysis evaluating the ability of eGFR equations to identify progression to CKD stage 4+.

Note that in each of the following tables the number of patients tested each year is equal to the total cohort minus the number of patients that have had a previous TP or delayed positive result (following a missed true progression event).

Table 5. 10-year clinical accuracy simulation results: MDRD equation, CKD stage shift (into stage 4+) progression criteria.

Year	% Tested[a] (out of total cohort)	% Positive (out of all tested)	% FPs (out of all positives)	% TP (out of all positives)	% Negative (out of all tested)	% FN (out of all negatives)	FN: average delay (years)	FN: % never identified (out of FNs)	Sensitivity (cumulative)	Specificity (cumulative)
Year 1	100.0% [100 – 100]	8.7% [7.4 – 10.1]	99.6% [96.1 – 100]	0.4% [0.0 – 3.9]	91.3% [89.9 – 92.6]	2.9% [1.0 – 5.2]	1.7 [1.5 – 1.8]	33.6% [24.5 – 39.4]	1.9% [0.0 – 22.6]	91.1% [90.0 – 92.4]
Year 2	100.0% [99.6 – 100]	10.5% [9.5 – 11.6]	79.2% [68.8 – 84.8]	11.7% [5.5 – 22.2]	89.5% [88.4 – 90.5]	1.5% [0.7 – 2.9]	1.2 [1.0 – 1.7]	49.9% [30.0 – 60.8]	24.4% [11.0 – 36.2]	91.2% [90.3 – 92.5]
Year 3	97.8% [96.9 – 98.5]	12.7% [8.5 – 16.1]	70.8% [65.7 – 75.4]	19.4% [14.5 – 24.4]	87.3% [83.9 – 91.5]	3.8% [2.8 – 5.0]	2.1 [1.6 – 2.6]	28.7% [18.1 – 37.8]	33.8% [27.8 – 40.6]	90.9% [89.3 – 92.3]
Year 4	94.2% [92.8 – 96.1]	10.1% [7.3 – 15.3]	59.3% [53.5 – 65.2]	30.2% [23.1 – 35.8]	89.9% [84.7 – 92.7]	2.5% [1.1 – 4.9]	1.2 [1.1 – 1.3]	9.0% [0.0 – 18.0]	41.2% [34.8 – 46.3]	91.6% [90.8 – 92.5]
Year 5	90.3% [89.2 – 91.6]	12.3% [10.9 – 15.0]	73.6% [58.9 – 83.2]	5.2% [0.0 – 15.7]	87.7% [85.0 – 89.1]	1.8% [0.0 – 5.6]	1.9 [1.7 – 2.2]	21.2% [5.9 – 26.9]	40.0% [34.6 – 44.1]	91.4% [90.7 – 92.2]
Year 6	87.3% [84.6 – 89.9]	11.9% [10.5 – 14.4]	73.3% [61.0 – 81.2]	14.6% [9.8 – 16.9]	88.1% [85.6 – 89.5]	3.7% [2.4 – 5.6]	1.5 [1.4 – 1.7]	28.7% [23.8 – 32.9]	39.1% [34.7 – 42.6]	91.3% [90.6 – 92.0]
Year 7	84.5% [80.1 – 88.0]	11.3% [9.9 – 14.0]	58.6% [48.2 – 65.8]	23.2% [14.9 – 33.5]	88.7% [86.0 – 90.1]	5.8% [4.2 – 8.3]	1.5 [1.4 – 1.5]	40.4% [35.2 – 44.6]	37.8% [34.5 – 40.4]	91.5% [90.7 – 92.2]
Year 8	80.5% [75.5 – 84.7]	10.2% [8.8 – 13.2]	51.1% [43.7 – 61.0]	19.1% [12.5 – 28.6]	89.8% [86.8 – 91.2]	5.1% [3.4 – 8.1]	1.4 [1.3 – 1.4]	37.5% [34.2 – 42.3]	36.5% [33.5 – 38.9]	91.7% [90.8 – 92.5]
Year 9	76.6% [71.1 – 81.3]	8.9% [7.5 – 12.2]	50.9% [37.6 – 62.0]	13.4% [2.6 – 32.9]	91.1% [87.8 – 92.5]	3.4% [0.7 – 7.6]	1.0 [1.0 – 1.0]	64.1% [58.8 – 70.1]	35.7% [32.7 – 38.2]	92.1% [91.0 – 92.8]
Year 10	73.2% [67.8 – 77.3]	7.9% [6.4 – 11.0]	56.3% [46.0 – 67.5]	6.6% [0.0 – 16.4]	92.1% [89.0 – 93.6]	1.4% [0.0 – 3.5]	NA	100.0% [100 – 100]	35.5% [32.7 – 37.8]	92.3% [91.1 – 93.1]

Table 6. 10-year clinical accuracy simulation results: CKD-EPI$_{creatinine}$ equation, CKD stage shift (into stage 4+) progression criteria.

Year	% Tested[a] (out of total cohort)	% Positive (out of all tested)	% FPs (out of all positives)	% TP (out of all positives)	% Negative (out of all tested)	% FN (out of all negatives)	FN: average delay (years)	FN: % never identified (out of FNs)	Sensitivity (cumulative)	Specificity (cumulative)
Year 1	100.0% [100 – 100]	8.4% [7.0 – 9.8]	99.5% [95.0 – 100]	0.5% [0.0 – 5.0]	91.6% [90.2 – 93.0]	2.9% [0.9 – 5.2]	1.7 [1.5 – 1.8]	35.9% [25.1 – 42.2]	2.8% [0.0 – 27.9]	91.4% [90.3 – 92.8]
Year 2	100.0% [99.5 – 100]	10.3% [9.4 – 11.4]	79.0% [68.5 – 84.5]	12.0% [5.7 – 22.7]	89.7% [88.6 – 90.6]	1.5% [0.7 – 2.9]	1.2 [1.0 – 1.7]	52.9% [32.6 – 63.0]	24.9% [11.1 – 37.8]	91.5% [90.6 – 92.8]
Year 3	97.8% [96.9 – 98.5]	13.2% [7.8 – 17.1]	73.7% [68.5 – 77.7]	17.1% [13.1 – 21.0]	86.8% [82.9 – 92.2]	4.1% [3.0 – 5.3]	2.1 [1.5 – 2.6]	26.9% [16.2 – 38.3]	32.2% [27.0 – 37.6]	90.9% [89.1 – 92.4]
Year 4	94.4% [93.0 – 96.4]	9.8% [6.9 – 15.2]	57.5% [50.2 – 64.6]	30.4% [24.3 – 37.1]	90.2% [84.8 – 93.1]	2.6% [1.0 – 5.3]	1.2 [1.1 – 1.4]	11.8% [0.0 – 22.2]	39.6% [34.1 – 44.1]	91.6% [90.7 – 92.6]
Year 5	90.5% [89.3 – 91.8]	12.0% [10.6 – 14.6]	72.8% [57.8 – 82.8]	5.3% [0.0 – 16.1]	88.0% [85.4 – 89.4]	1.8% [0.0 – 5.5]	1.9 [1.7 – 2.2]	20.8% [5.9 – 26.5]	38.7% [34.0 – 43.1]	91.5% [90.8 – 92.3]
Year 6	87.5% [84.9 – 90.0]	11.6% [10.3 – 14.0]	72.5% [59.3 – 80.8]	14.9% [9.9 – 20.1]	88.4% [86.0 – 89.7]	3.6% [2.4 – 5.5]	1.5 [1.4 – 1.7]	25.8% [21.9 – 29.6]	38.0% [34.3 – 41.5]	91.4% [90.7 – 92.2]
Year 7	84.7% [80.4 – 88.1]	11.1% [9.7 – 13.6]	57.1% [46.9 – 64.6]	23.9% [15.6 – 34.2]	88.9% [86.4 – 90.3]	5.7% [4.1 – 8.2]	1.5 [1.4 – 1.5]	36.3% [32.2 – 39.8]	37.1% [34.3 – 39.9]	91.6% [90.9 – 92.4]
Year 8	80.6% [75.6 – 84.7]	10.1% [8.7 – 12.9]	49.0% [41.4 – 59.3]	19.3% [12.7 – 28.9]	89.9% [87.1 – 91.3]	5.1% [3.4 – 8.1]	1.4 [1.3 – 1.4]	36.3% [33.3 – 39.8]	35.9% [33.4 – 38.3]	91.9% [91.1 – 92.7]
Year 9	76.5% [71.1 – 81.2]	8.8% [7.4 – 11.9]	48.6% [35.3 – 59.5]	13.8% [2.7 – 33.6]	91.2% [88.1 – 92.6]	3.4% [0.7 – 7.6]	1.0 [1.0 – 1.0]	63.6% [58.3 – 69.2]	35.2% [32.6 – 37.1]	92.2% [91.2– 93.0]
Year 10	73.1% [67.7 – 77.2]	7.7% [6.3 – 10.9]	54.0% [43.6 – 65.4]	6.9% [0.0 – 16.8]	92.3% [89.1 –]	1.4% [0.0 – 3.5]	NA [–]	100.0% [100 – 100]	35.0% [32.5 – 36.9]	92.5% [91.4 – 93.3]

Table 7. 10-year clinical accuracy simulation results: CKD-EPI$_{cystatin}$ equation, CKD stage shift (into stage 4+) progression criteria.

Year	% Tested[a] (out of total cohort)	% Positive (out of all tested)	% FPs (out of all positives)	% TP (out of all positives)	% Negative (out of all tested)	% FN (out of all negatives)	FN: average delay (years)	FN: % never identified (out of FNs)	Sensitivity (cumulative)	Specificity (cumulative)
Year 1	100.0% [100 – 100]	10.5% [8.7 – 12.0]	99.2% [95.7 – 100]	0.8% [0.0 – 4.3]	89.5% [88.0 – 91.3]	2.9% [0.7 – 5.3]	1.9 [1.7 – 2.0]	40.2% [30.1 – 44.1]	5.8% [0.0 – 29.8]	89.3% [87.6 – 91.3]
Year 2	99.9% [99.6 – 100]	13.2% [12.4 – 13.9]	88.8% [83.3 – 92.2]	6.4% [3.2 – 12.2]	86.8% [86.1 – 87.6]	2.0% [1.0 – 3.8]	1.2 [1.0 – 1.7]	52.0% [36.5 – 60.3]	18.5% [7.6 – 31.6]	88.6% [87.5 – 89.9]
Year 3	98.4% [97.9 – 98.9]	19.6% [13.0 – 27.9]	78.2% [72.8 – 84.2]	14.0% [10.1 – 18.0]	80.4% [72.1 – 87.0]	3.8% [2.7 – 4.9]	2.7 [1.8 – 3.2]	53.4% [41.1 – 62.9]	33.1% [29.1 – 38.3]	86.9% [83.6 – 89.1]
Year 4	94.3% [92.8 – 96.1]	11.7% [9.1 – 15.8]	80.7% [65.3 – 97.2]	16.9% [2.8 – 28.8]	88.3% [84.2 – 90.9]	3.6% [2.2 – 5.6]	1.5 [1.3 – 1.7]	41.9% [31.4 – 55.1]	34.9% [26.0 – 43.2]	87.7% [85.2 – 89.4]
Year 5	92.0% [90.7 – 93.7]	12.6% [11.2 – 15.0]	79.6% [66.0 – 88.3]	4.7% [0.0 – 14.2]	87.4% [85.0 – 88.8]	1.8% [0.0 – 5.7]	2.0 [1.8 – 2.3]	32.4% [15.1 – 39.1]	33.9% [26.0 – 39.4]	88.1% [86.1 – 89.5]
Year 6	89.6% [86.4 – 92.3]	12.1% [11.0 – 14.1]	75.9% [65.2 – 82.3]	13.0% [8.7 – 17.4]	87.9% [85.9 – 89.0]	3.7% [2.5 – 5.6]	1.6 [1.5 – 1.7]	39.0% [34.6 – 43.2]	33.7% [27.3 – 37.8]	88.4% [86.8 – 89.6]
Year 7	87.0% [82.4 – 90.3]	11.1% [10.0 – 13.3]	62.3% [52.6 – 68.6]	21.2% [14.0 – 30.6]	88.9% [86.7 – 90.0]	5.8% [4.2 – 8.3]	1.5 [1.4 – 1.6]	44.8% [41.7 – 47.6]	33.1% [28.6 – 36.3]	88.9% [87.6 – 90.0]
Year 8	83.3% [78.2 – 87.2]	10.0% [8.8 – 12.5]	54.8% [47.9 – 63.7]	17.4% [11.7 – 25.9]	90.0% [87.5 – 91.2]	5.1% [3.4 – 8.0]	1.4 [1.3 – 1.4]	45.4% [42.0 – 48.5]	32.3% [28.1 – 35.5]	89.5% [88.3 – 90.5]
Year 9	79.6% [74.2 – 84.0]	8.7% [7.5 – 11.6]	54.7% [42.0 – 63.8]	12.5% [2.5 – 29.9]	91.3% [88.4 – 92.5]	3.3% [0.7 – 7.6]	1.0 [1.0 – 1.0]	67.4% [62.1 – 72.5]	31.8% [27.8 – 35.2]	90.0% [89.0 – 91.0]
Year 10	76.5% [71.1 – 80.4]	7.7% [6.5 – 10.6]	59.2% [50.3 – 68.3]	6.3% [0.0 – 15.2]	92.3% [89.4 – 93.5]	1.3% [0.0 – 3.3]	NA	100.0% [100 – 100]	31.7% [27.9 – 35.0]	90.4% [89.6 – 91.4]

Table 8. 10-year clinical accuracy simulation results: CKD-EPI$_{cystatin-creatinine}$ equation, CKD stage shift (into stage 4+) progression criteria.

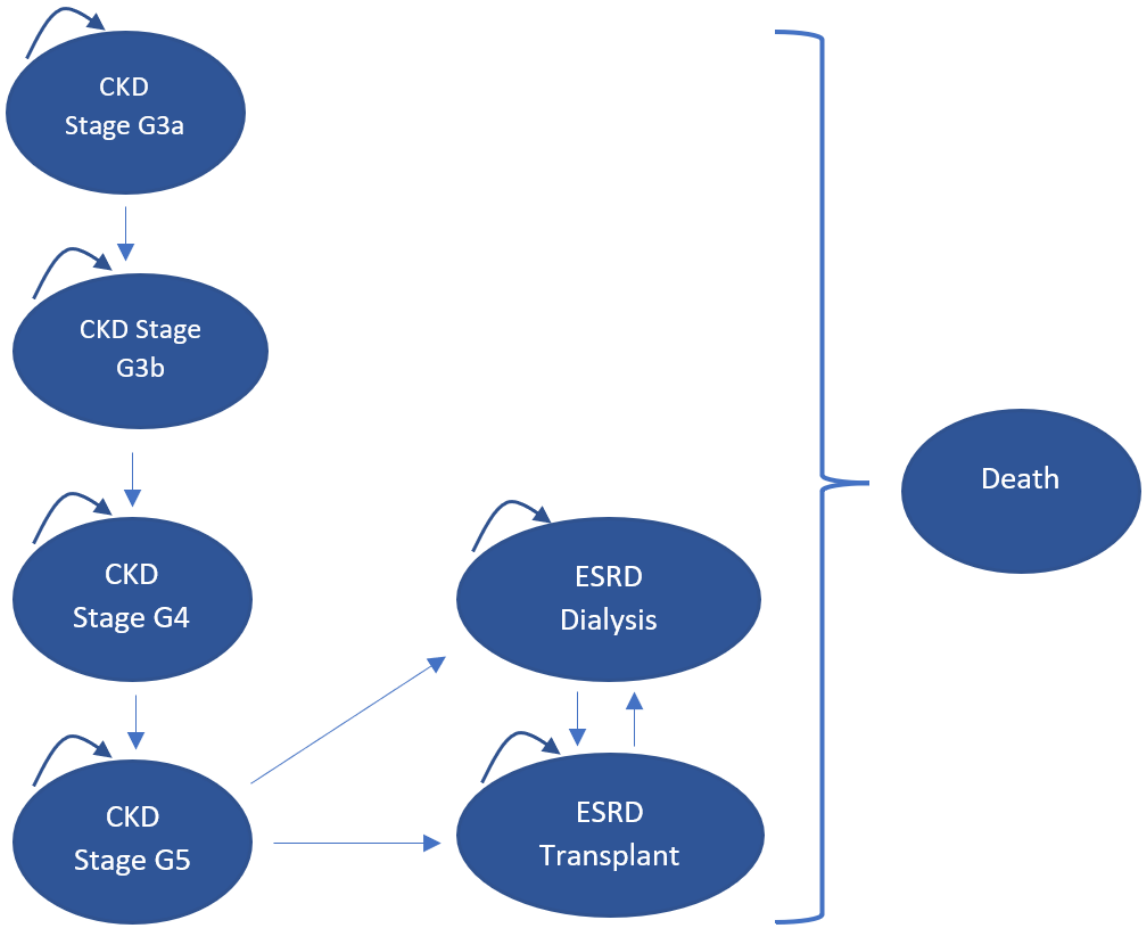
Year	% Tested[a] (out of total cohort)	% Positive (out of all tested)	% FPs (out of all positives)	% TP (out of all positives)	% Negative (out of all tested)	% FN (out of all negatives)	FN: average delay (years)	FN: % never identified (out of FNs)	Sensitivity (cumulative)	Specificity (cumulative)
Year 1	100.0% [100 – 100]	8.9% [7.3 – 10.5]	99.4% [93.6 – 100]	0.6% [0.0 – 6.4]	91.1% [89.6 – 92.7]	2.9% [0.9 – 5.2]	1.6 [1.4 – 1.7]	52.1% [39.5 – 57.7]	3.3% [0.0 – 34.8]	90.9% [89.1 – 92.5]
Year 2	99.9% [99.4 – 100]	11.0% [10.2 – 11.7]	84.0% [75.8 – 88.4]	9.6% [4.6 – 18.4]	89.0% [88.3 – 89.8]	1.7% [0.8 – 3.3]	1.1 [1.0 – 1.6]	65.3% [50.5 – 73.7]	21.8% [9.3 – 35.3]	90.7% [89.5 – 92.0]
Year 3	98.2% [97.4 – 98.7]	20.9% [10.7 – 30.8]	82.2% [77.2 – 88.0]	12.7% [8.8 – 16.3]	79.1% [69.2 – 89.3]	4.1% [2.8 – 5.4]	2.5 [1.5 – 3.1]	61.2% [39.7 – 72.6]	33.4% [28.9 – 37.9]	87.7% [84.0 – 90.9]
Year 4	94.7% [93.3 – 96.3]	10.1% [7.4 – 14.7]	62.5% [53.8 – 73.4]	34.6% [25.3 – 42.0]	89.9% [85.3 – 92.6]	2.0% [0.7 – 4.6]	1.1 [1.1 – 1.3]	23.7% [0.0 – 39.9]	43.6% [38.2 – 48.2]	89.0% [86.4 – 90.9]
Year 5	91.1% [90.0 – 92.4]	11.3% [9.9 – 13.7]	78.9% [63.8 – 88.7]	5.4% [0.0 – 16.5]	88.7% [86.3 – 90.1]	1.8% [0.0 – 5.6]	1.9 [1.7 – 2.2]	38.3% [20.1 – 45.9]	42.1% [37.9 – 46.5]	89.4% [87.3 – 90.9]
Year 6	88.8% [85.9 – 91.3]	11.0% [9.7 – 12.9]	75.8% [63.9 – 83.1]	15.5% [10.5 – 20.4]	89.0% [87.1 – 90.3]	3.6% [2.4 – 5.4]	1.4 [1.3 – 1.6]	46.2% [41.2 – 51.0]	40.8% [37.4 – 44.3]	89.7% [87.9 – 91.0]
Year 7	86.5% [82.2 – 89.7]	10.1% [8.9 – 12.1]	59.4% [48.8 – 66.7]	24.8% [15.9 – 35.0]	89.9% [87.9 – 91.1]	5.7% [4.1 – 8.0]	1.4 [1.3 – 1.5]	53.9% [49.9 – 56.9]	38.9% [36.5 – 41.6]	90.1% [88.7 – 91.3]
Year 8	82.9% [78.2 – 86.7]	8.6% [7.5 – 11.2]	51.9% [43.7 – 62.7]	21.0% [13.8 – 31.2]	91.4% [88.8 – 92.5]	5.0% [3.3 – 7.9]	1.4 [1.3 – 1.4]	47.8% [44.6 – 51.4]	37.3% [34.8 – 39.6]	90.7% [89.4 – 91.8]
Year 9	79.5% [74.4 – 83.9]	7.3% [6.1 – 10.2]	51.4% [36.0 – 63.0]	15.1% [2.9 – 36.4]	92.7% [89.8 – 93.9]	3.3% [0.7 – 7.4]	1.0 [1.0 – 1.0]	67.8% [62.8 – 72.7]	36.3% [33.7 – 38.3]	91.2% [90.1 – 92.2]
Year 10	76.7% [71.6 – 80.5]	6.4% [5.3 – 9.3]	56.1% [45.0 – 67.8]	7.7% [0.0 – 18.8]	93.6% [90.7 – 94.7]	1.3% [0.0 – 3.2]	NA	100.0% [100 – 100]	36.1% [33.7 – 38.0]	91.6% [90.7 – 92.6]

S2.3. Modelling longer-term costs and outcomes

In anticipation of cystatin C-based eGFR equations demonstrating an improvement in the sensitivity, we developed a Markov model structure in R to capture the impact of identifying individuals whose CKD is progressing earlier. We would like to make this model freely available for future research (the code is publicly available on Github: https://github.com/bshinkins/eGFR-C, accessed 27th July 2023) as it may be useful in two key contexts: 1) if a more sensitive means of detecting progression is identified, and 2) if a novel intervention for preventing or delaying progression in individuals with CKD category 3a/b is found. We have not included cost parameters as these will be highly dependent on the intervention(s) evaluated and need to be relevant to the costing year.

Model Structure and Transition Probabilities

Figure 1. Markov model structure.



The Markov model is designed to capture costs and outcomes over the lifetime of the cohort and transitions between health states are captured annually, in line with previous economic evaluations in CKD.[1] The model structure and parameterisation were developed in line with the findings from a recent systematic review of economic models in CKD,[1] although we have added the additional split between stage G3a and stage G3b in line with the latest KDIGO guidelines (see Figure 32 and Table 53).[2] The model can be used to represent individuals with CKD followed up in primary care or secondary care. For example, starting probabilities could be based on the stage at which individuals were referred to a specialist nephrologist or at the point accelerated progression is identified. It should be noted though that there was considerable heterogeneity in the probability transition estimates identified in the literature and none of the included studies reported transitions for a routinely monitored UK patient population. More relevant data should be possible to obtain as UK cohort data matures from studies such as OxRen[3] and the UK Renal Registry.

Since the development of this model structure, a number of cohort studies have published evidence demonstrating that a significant proportion of individuals with CKD progress and regress. For example, results from a population-based cohort study of adults with CKD in Alberta, Canada, estimate that the 5-year probability of regression was similar to that of progression or kidney failure in mild, moderate and severe CKD.[4] Similarly, the Oxford Renal Cohort study based in the UK, demonstrated that 24% of people evidenced rapid GFR decline whereas 21% evidenced remission of CKD.[5] We also found this to be the case in the eGFR-C cohort (see section 1.4.1.2). This brings to question the current model structure used here and more generally to capture CKD progression, which fails to capture CKD regression. This is a relatively straightforward adjustment, however.

Table 9. Suggested annual transition probability parameters (to be updated/adapted for use).

Start:	**Move to:**	**Estimate**	**Distribution**	**Source**
Stage G3a	Stage G3b	0.096	Beta(228.42,1438.88)	Elbasha et al 2017[1]
Stage G3b	Stage G4	0.137	Beta(110.09,1249.03)	
Stage G4	Stage G5	0.081	Beta(126.69,75.69)	
Stage G5	Dialysis	0.626	Beta(77.08,8487.72)	
Stage G5	Transplant	0.009	Beta(67.16,3467.81)	
Dialysis	Transplant	0.019	Beta(19.34,401.12)	
Transplant	Dialysis	0.046	Beta(105,867.26)	
Start	**Move to**	**Hazard Rate**	**Distribution**	**Source**
Stage G3a	Death	1.20	LogNormal(0.18,0.02)	Elbasha et al 2017[1]
Stage G3b	Death	1.80	LogNormal(0.59,0.03)	Elbasha et

				al 2017[1]
Stage G4	Death	3.20	LogNormal(1.16,0.02)	Elbasha et al 2017[1]
Stage G5	Death	5.90	LogNormal(1.77,0.05)	Elbasha et al 2017[1]
Dialysis	Death	0.177	Min, Max (0.008,0.626)	Elbasha et al 2017[1]
Transplant	Death	0.053	Min, Max (0.012,0.093)	Elbasha et al 2017[1]

Health-related quality of life

Cooper et al conducted a systematic review of health-related quality of life (HRQoL) utility weights for different stages of chronic kidney disease.[6] The vast majority of studies identified reported HRQoL data for those who have already reached ESRD. Two studies were identified that report data for stage G3 CKD, one of which used the EQ-5D-3L questionnaire to measure HRQoL and broke the results down by G3a and G3b (although no difference was found).[7] The HRQoL parameters used in the model can be found in Table 54. When selecting which parameters to use in our model, we prioritised those which used EQ5D to measure HRQoL for consistency and UK-based studies where available.

Table 10. Suggested utility parameters (to be updated/adapted for use).

CKD Stage	**Utility (Distribution)**	**Instrument, country (sample size)**	**Source**
CKD Stage G3a	0.80 (95% CI: 0.69-1)	EQ-5D-3L, UK (n=45)	Jesky et al (2016)[7]
CKD Stage G3b	0.80 (95% CI: 0.68-1)	EQ-5D-3L, UK (n=173)	
CKD Stage G4	0.74 (95% CI: 0.62-0.85)	EQ-5D-3L, UK (n=423)	
CKD Stage G5	0.73 (95% CI: 0.62-1)	EQ-5D-3L, UK (n=75)	
Haemodialysis	0.565 Beta (204.85, 157.72)	EQ-5D-3L, various (systematic review)	Liem et al (2008)[8]
Post-transplant	0.827 Beta (809.58, 169.36)	EQ-5D-5L, UK (n=512)	Li et al (2017)[9]

We have not provided starting probabilities and costs because these will be heavily dependent on the research question, country and perspective of the analysis

Summary

We welcome adaptation of our R code for future research, but we recommend that the model structure is reviewed in light of new evidence suggesting that a significant proportion of those with CKD regress. We also recommend that, as UK renal cohort data matures, that the transition probability estimates are reviewed to ensure that they are representative of those monitored in routine UK clinical practice.

References

1. Elbasha E, Greaves W, Roth D, Nwankwo C. Cost-effectiveness of elbasvir/grazoprevir use in treatment-naive and treatment-experienced patients with hepatitis C virus genotype 1 infection and chronic kidney disease in the United States. J Viral Hepat. 2017;24:268-79.

2. Kidney Disease Improving Global Outcomes (KDIGO). Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International supplements 2013;3:1-150.

3. Hill NR, Lasserson D, Fatoba S, O'Callaghan CA, Pugh C, Perera-Salazar R*, et al.* The Oxford Renal (OxRen) cross-sectional study of chronic kidney disease in the UK. BMJ Open. 2013;3:e004265.

4. Liu P, Quinn RR, Lam NN, Al-Wahsh H, Sood MM, Tangri N*, et al.* Progression and Regression of Chronic Kidney Disease by Age Among Adults in a Population-Based Cohort in Alberta, Canada. JAMA Netw Open. 2021;4:e2112828.

5. Hirst JA, Taal MW, Fraser SD, Mena JMO, O'Callaghan CA, McManus RJ*, et al.* Change in glomerular filtration rate over time in the Oxford Renal Cohort Study: observational study. Br J Gen Pract. 2022;72:e261-e8.

6. Cooper JT, Lloyd A, Sanchez JJG, Sorstadius E, Briggs A, McFarlane P. Health related quality of life utility weights for economic evaluation through different stages of chronic kidney disease: a systematic literature review. Health Qual Life Outcomes. 2020;18:310.

7. Jesky MD, Dutton M, Dasgupta I, Yadav P, Ng KP, Fenton A*, et al.* Health-Related Quality of Life Impacts Mortality but Not Progression to End-Stage Renal Disease in Pre-Dialysis Chronic Kidney Disease: A Prospective Observational Study. PLoS One. 2016;11:e0165675.

8. Liem YS, Bosch JL, Hunink MG. Preference-based quality of life of patients on renal replacement therapy: a systematic review and meta-analysis. Value Health. 2008;11:733-41.

9. Li B, Cairns JA, Draper H, Dudley C, Forsythe JL, Johnson RJ*, et al.* Estimating Health-State Utility Values in Kidney Transplant Recipients and Waiting-List Patients Using the EQ-5D-5L. Value Health. 2017;20:976-84.