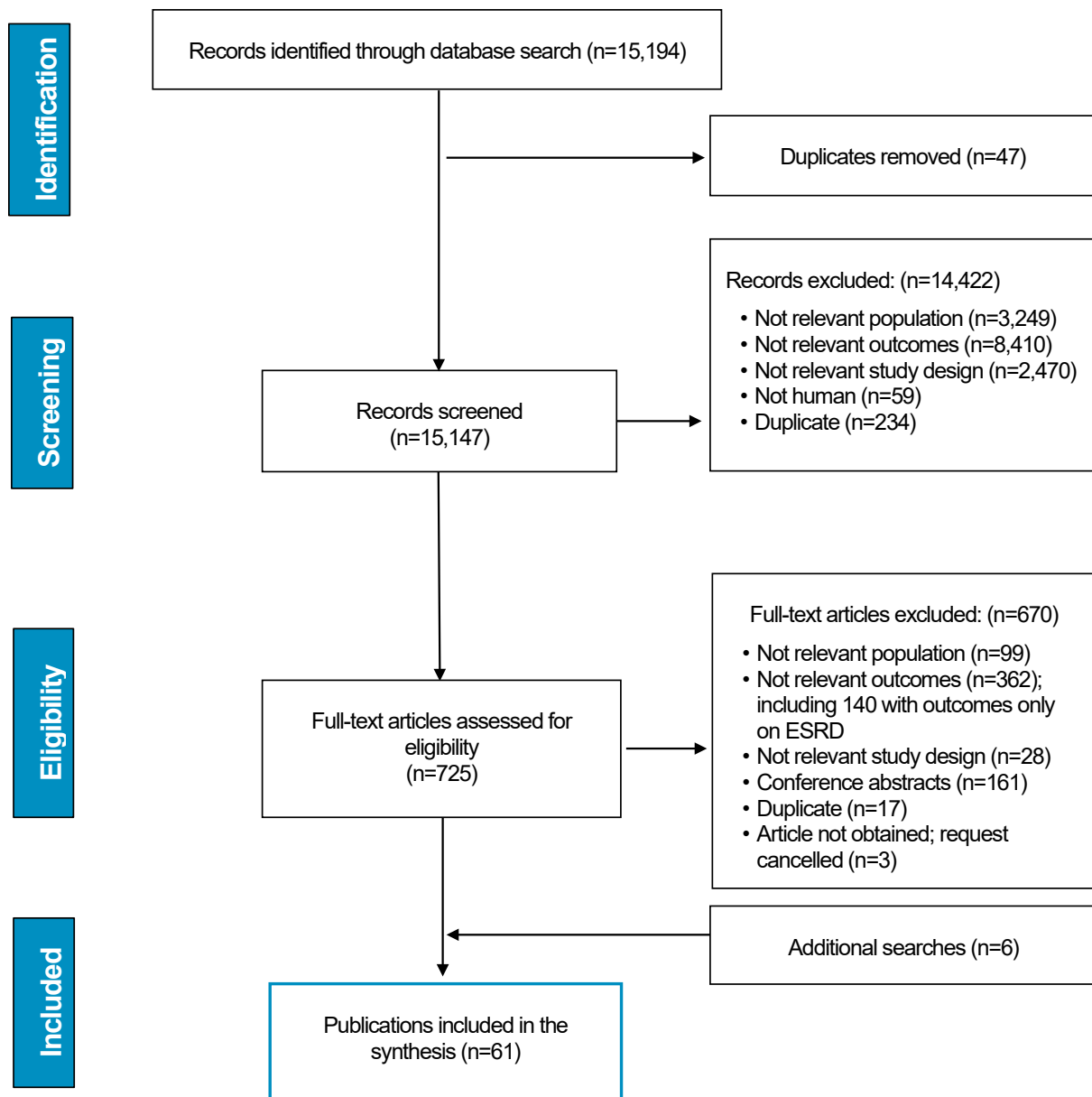


From a supplement to *The American Journal of Managed Care*<sup>®</sup>: “Patients With Diabetes and Chronic Kidney Disease: ACE Inhibitor or ARB Treatment, Medical Costs for Disease Management, and the FINE-CKD Model to Evaluate Economic Value of Finerenone”

**eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes**

Michał T. Pochopień, MSc; David Z. I. Cherney, MD, PhD; Kerstin Folkerts, MSc; Pierre Levy, PhD; Aurélie Millier, PhD; Stephen Morris, PhD; Prabir Roy-Chaudhury, MD, PhD; Sean D. Sullivan, PhD; Paul Mernagh, MCom

**eAppendix Figure 1. FINE-CKD Model PRISMA Diagram**



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**eAppendix Table 1.** Search Strategy Run in Medline and Embase via the OVID Interface<sup>a</sup>

#	PICOS	Searches	Results
1	Population (P)	chronic kidney disease/ or Chronic kidney failure/ or end stage renal disease/ or (CKD or ESRD or CKF or CRF or ESKD or ESKF or ESRF).mp.	343,762
2		renal insufficiency, chronic/ or kidney failure, chronic/	164,571
3		diabetic nephropath\$.mp. or diabetic nephropathy/	78,216
4		((Chronic\$ or end-stage or end stage or "stage 5" or "stage five") adj2 (renal or kidney\$) adj2 (failure\$ or disease\$ or disorder\$ or insufficien\$)).mp.	386,272
5		(diabetic adj2 (kidney* or renal*) adj2 disease*).mp.	8101
6		1 or 2 or 3 or 4 or 5	483,513
7	Models	Socioeconomics/	137,766
8		Cost effectiveness analysis/	229,456
9		Cost-benefit analysis/	163,948
10		"deductibles and coinsurance"/	59,714
11		Health care financing/	13,218
12		Health economics/	32,582
13		Value of life/	13,7043
14		(fiscal or financial or finance or funding).tw.	337,348
15		Cost minimization analysis/	51,853
16		(cost adj variable\$).mp.	417

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17		exp economics, medical/	84,9315
18		Economics, pharmaceutical/	10,192
19		exp budgets/	42,385
20		(Cost-effectiveness or cost-effectiveness).tw.	141,435
21		(cost adj estimate\$).mp.	5612
22		(QALY or QALYs).tw.	29,606
23		(Quality?adjusted adj3 life\$).mp.	441
24		Incremental cost.tw.	29,756
25		Cost?benefit.tw.	293
26		(cost or costs or costly or costing\$).ti.	256,096
27		"costs and cost analysis"/	101,053
28		Financial management/	128,797
29		Health expenditures/	186,484
30		exp "fees and charges"/	69,942
31		or/7-30	1,652,483
32	P+Models	6 and 31	17,634
33		limit 32 to yr="1860 - 2008"	5604
34		limit 32 to yr="2009 - 2013"	4050
35		limit 32 to yr="2014 - 2017"	4697

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36		limit 32 to yr="2018 -Current"	3265
37		33 or 34 or 35 or 36	17,616
38		32 not 37	18
39		remove duplicates from 33	4493
40		remove duplicates from 34	3451
41		remove duplicates from 35	3992
42		remove duplicates from 36	2794
43		remove duplicates from 38	18
44	Final result	39 or 40 or 41 or 42 or 43	14,748

\*Search strategy run in Medline and Embase via the OVID interface on April 15, 2020.

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**eAppendix Table 2.** Search Strategy for Economic Evaluations: NHS EED, HTA, and DARE Databases (access via the crd.york website)<sup>a</sup>

Line	Search	Hits
1	MeSH DESCRIPTOR kidney failure, chronic EXPLODE ALL TREES	415
2	(chronic kidney disease or Chronic kidney failure or end stage renal disease or (CKD or ESRD or CKF or CRF or ESKD or ESKF or ESRF))	626
3	MeSH DESCRIPTOR renal insufficiency, chronic EXPLODE ALL TREES	538
4	(diabetic nephropath* or diabetic nephropathy)	138
5	((Chronic* or end-stage or end stage or "stage 5" or "stage five") adj2 (renal or kidney\$) near2 (failure* or disease* or disorder* or insufficien*))	427
6	((diabetic near2 (kidney* or renal*) near2 disease*))	32
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	1039
8	(Socioeconomics)	1
9	(Cost effectiveness analysis)	8784
10	MeSH DESCRIPTOR Cost-benefit analysis EXPLODE ALL TREES	13,213
11	(deductibles and coinsurance)	4
12	(Health care financing)	78
13	(Health economics)	601
14	MeSH DESCRIPTOR Value of life EXPLODE ALL TREES	117
15	((fiscal or financial or finance or funding))	2915
16	(Cost minimization analysis)	82
17	(cost near variable*)	203

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18	MeSH DESCRIPTOR economics, medical EXPLODE ALL TREES	53
19	MeSH DESCRIPTOR Economics, pharmaceutical EXPLODE ALL TREES	199
20	MeSH DESCRIPTOR budgets EXPLODE ALL TREES	54
21	(Cost-effectiveness or cost-effectiveness)	15,894
22	(cost near estimate*)	3175
23	(QALY or QALYs)	3263
24	(Quality*adjusted near3 life*)	0
25	((Quality adjusted or Quality-adjusted) near3 life*)	5304
26	(Incremental cost)	4390
27	(Cost benefit or cost-benefit)	13,517
28	(cost or costs or costly or costing*)	24,129
29	(costs and cost analysis)	4656
30	MeSH DESCRIPTOR Financial management EXPLODE ALL TREES	123
31	MeSH DESCRIPTOR Health expenditures EXPLODE ALL TREES	213
32	MeSH DESCRIPTOR fees and charges EXPLODE ALL TREES	290
33	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32	25,317
34	#7 AND #33	446
35	(#34) IN DARE, NHSEED, HTA	446

\*Search was run on April 15, 2020, in NHS EED, HTA, and DARE databases (access via the crd.york website)

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**eAppendix Table 3.** Overview Of Cost-effectiveness Models Among Patients With CKD

Author, year, country	Study population (eg eGFR, albuminuria, ACE/ARB)	Model summary (type, time horizon, cycle length, perspective)	Health states /events and adverse events list	Treatment arms	Transition probability sources	Efficacy measures	Utility types and source	Discount rate for cost	Discount rate for effect
Evans, et al <sup>24</sup> UK	Cohort of CKD stage 3a patients •eGFR (mL/min/1.73m <sup>2</sup> ): 52.5 •Albuminuria: NR •ACE/ARB: NR	<ul style="list-style-type: none"> <li>• Type: Patient-level simulation model</li> <li>• Time horizon: Lifetime</li> <li>• Cycle length: 1 month</li> <li>• Perspective: UK health care payer</li> </ul>	<p><u>Health states:</u></p> <ul style="list-style-type: none"> <li>• CKD 3a</li> <li>• CKD 3b</li> <li>• CKD 4</li> <li>• CKD 5</li> <li>• Dead</li> <li>• Dialysis</li> <li>• Transplant</li> </ul> <p>Events:</p> <ul style="list-style-type: none"> <li>• Acute hyperkalaemia</li> <li>• Arrhythmia</li> <li>• CV event</li> <li>• Hospitalization</li> <li>• Change in RAASi use</li> </ul> <p><u>Adverse events:</u></p> <p>MACE</p>	<ul style="list-style-type: none"> <li>• Maintaining normokalaemia and optimising RAASi therapy</li> <li>• No RAASi</li> </ul>	<ul style="list-style-type: none"> <li>• Evans et al, 2012</li> <li>• Hoerger et al, 2010</li> <li>• Orlando et al, 2011</li> <li>• Gandjour et al, 2015</li> <li>• UK Renal Registry</li> </ul>	<ul style="list-style-type: none"> <li>• QALY</li> <li>• LY</li> </ul>	<p>Type: NR</p> <p>Source:</p> <ul style="list-style-type: none"> <li>•Gorodetskaya et al, 2005</li> <li>•Lee et al, 2005</li> </ul>	3.5%	3.5%
Schlackow, et al <sup>25</sup> UK and USA	Patients with moderate to	<ul style="list-style-type: none"> <li>• Type: Markov model</li> </ul>	<p><u>Health states:</u></p> <ul style="list-style-type: none"> <li>•CKD submodel:</li> </ul>	<ul style="list-style-type: none"> <li>• Atorvastatin 40 mg</li> </ul>	<ul style="list-style-type: none"> <li>• Baigent et al, 2011</li> <li>• SHARP trial</li> </ul>	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	Type: Indirect (EQ-5D-3L)	<ul style="list-style-type: none"> <li>• USA: 3%</li> </ul>	<ul style="list-style-type: none"> <li>• USA: 3%</li> </ul>

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	<p>advanced NDD-CKD</p> <ul style="list-style-type: none"> <li>• <u>eGFR</u> (ml/min/1.73 m<sup>2</sup>): <ul style="list-style-type: none"> <li>• Stage 3a: 60-45</li> <li>• Stage 3b: 30 &lt;eGFR &lt;45</li> <li>• Stage 4: 15 &lt; eGFR &lt;30</li> <li>• Stage 5: eGFR &lt;15</li> </ul> </li> <li>• <u>Albuminuria</u>: NR</li> <li>• <u>ACE/ARB</u>: NR</li> </ul>	<ul style="list-style-type: none"> <li>• Time horizon: Lifetime</li> <li>• Cycle length: NR</li> <li>• Perspective: Health care system</li> </ul>	<ul style="list-style-type: none"> <li>• CKD stage 3b</li> <li>• CKD stage 4</li> <li>• CKD stage 5 not on RRT</li> <li>• Dialysis</li> <li>• Transplant</li> <li>• CVD submodel: <ul style="list-style-type: none"> <li>• Nonvascular death</li> <li>• Vascular death</li> <li>• Nonfatal MAE</li> <li>• Nonfatal haemorrhagic stroke</li> </ul> </li> </ul> <p><u>Adverse events:</u> Base case: Not included SA: Yes</p> <ul style="list-style-type: none"> <li>• Adverse effects on muscle (eg, myopathy and rhabdomyolysi)</li> <li>• Adverse effects on diabetes</li> </ul>	<ul style="list-style-type: none"> <li>• Ezetimibe 10 mg plus atorvastatin 40 mg</li> <li>• Atorvastatin 20mg daily</li> <li>• no LDL-C lowering treatment</li> </ul>			<p>Source:</p> <ul style="list-style-type: none"> <li>• SHARP trial</li> <li>• Schlackow et al, 2017</li> </ul>	<ul style="list-style-type: none"> <li>• UK: 3.5%</li> </ul>	<ul style="list-style-type: none"> <li>• UK: 3.5%</li> </ul>
Campbell, et al <sup>26</sup>	Patients diagnosed with stage 4 or 5	<ul style="list-style-type: none"> <li>• Type: Discrete event</li> </ul>	<u>Health states:</u>	• Screening with the TST	Karnon et al, 2012	QALY	Type: Indirect (SF-6D)	1.5%	1.5%



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Canada	<p>CKD not requiring dialysis (late-stage CKD) and those who began dialysis therapy</p> <ul style="list-style-type: none"> <li>• <u>eGFR</u> (ml/min/1.73 m<sup>2</sup>): NR</li> <li>• <u>Albuminuria</u>: NR</li> <li>• <u>ACE/ARB</u>: NR</li> </ul>	<p>simulation model</p> <ul style="list-style-type: none"> <li>• Time horizon: 5 years</li> <li>• Cycle length: NR</li> <li>• Perspective: Health care system</li> </ul>	<ul style="list-style-type: none"> <li>• Late-stage CKD</li> <li>• Tuberculosis</li> <li>• Dialysis</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Yes/NR</p>	<ul style="list-style-type: none"> <li>• IGRA</li> <li>• No LTBI screening</li> </ul>		<p>Sources:</p> <ul style="list-style-type: none"> <li>• Davison et al, 2009</li> <li>• Yang et al, 2015</li> <li>• Bauer et al, 2015</li> <li>• Hollan et al, 2009</li> <li>• Awan et al, 2011</li> </ul>			
Habbous, et al <sup>27</sup> Canada	<p>NDD- and DD-CKD patients</p> <ul style="list-style-type: none"> <li>• <u>eGFR</u> (ml/min/1.73 m<sup>2</sup>): NR</li> <li>• <u>Albuminuria</u>: NR</li> <li>• <u>ACE/ARB</u>: NR</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov model</li> <li>• Time horizon: Lifetime</li> <li>• Cycle length: 1 year</li> <li>• Perspective: Canadian health care system as public payer</li> </ul>	<p><u>Health states:</u></p> <ul style="list-style-type: none"> <li>• Scenario 1: <ul style="list-style-type: none"> <li>• NDD-CKD</li> <li>• DD-CKD</li> <li>• Death</li> </ul> </li> <li>• Scenario 2: <ul style="list-style-type: none"> <li>• DD-CKD</li> <li>• Death</li> </ul> </li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• Sevelamer</li> <li>• Lanthanum</li> <li>• Calcium-based binders</li> </ul>	<ul style="list-style-type: none"> <li>• O’Hare et al 2007</li> <li>• Neovius et al 2014</li> </ul>	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<p>Type: Indirect (NR)</p> <p>Source:</p> <ul style="list-style-type: none"> <li>• Wyld et al, 2012</li> <li>• Gorodetskaya et al, 2005</li> </ul>	1.5%	1.5%
Lin, et al <sup>28</sup> USA	<p>Medicare beneficiaries with stage 3 and 4 CKD between 45 and 84 years old</p> <ul style="list-style-type: none"> <li>• <u>eGFR</u> (ml/min/1.73 m<sup>2</sup>): 20-59 in 5 ml</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: Patients’ remaining lifetime</li> </ul>	<p><u>Health states:</u></p> <ul style="list-style-type: none"> <li>• Progressive CKD: <ul style="list-style-type: none"> <li>• eGFR 59</li> <li>• eGFR 55</li> <li>• eGFR 20</li> <li>• eGFR 15</li> <li>• eGFR 10</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• MDC program</li> <li>• SOC</li> </ul>	<ul style="list-style-type: none"> <li>• Van der Velde et al, 2011</li> <li>• Tangri et al, 2016</li> <li>• Arias 2015</li> <li>• United States Renal Data System. 2015</li> </ul>	<p>QALY</p>	<p>Type: Direct/indirect (TTO, SG, EQ-5D, 15D, or SF-6D or translated short-form surveys (SF-36 or</p>	3%	3%

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	<ul style="list-style-type: none"> <li>• <b>UACR</b> roughly 1, 300, 1,000, and 3,000 mg/g</li> <li>• <b>ACE/ARB</b>:NR</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Cycle length:</b> 1 month</li> <li>• <b>Perspective:</b> Third-party payer</li> </ul>	<ul style="list-style-type: none"> <li>• <b>eGFR 5</b></li> <li>• <b>ESRD</b></li> <li>• <b>Death</b></li> </ul> <p><u>Adverse events:</u> Not included/NR</p>				SF-12) into EQ-5D scores) Source: Wyld et al, 2012		
Pattanaprateep, et al <sup>29</sup> Thailand	<p>Diabetic and non-diabetic patients with CKD</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> CKD 1-5</li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> Patients were categorized as RAAS users if they used at least 1 RAAS blockade (ie., either ACEis or ARBs) for more than 3 months; otherwise, they were classified as non-RAAS users, which included patients who had never used ACEIs/ARBs or had used other antihypertensive drugs</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type:</b> Markov</li> <li>• <b>Time horizon:</b> 99 years</li> <li>• <b>Cycle length:</b> 1 year</li> <li>• <b>Perspective:</b> Societal</li> </ul>	<p><u>Health states:</u></p> <ul style="list-style-type: none"> <li>• CKD 1–4</li> <li>• ESRD</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• RAASi</li> <li>• No RAASi</li> </ul>	<ul style="list-style-type: none"> <li>• Vejakama et al, 2015</li> <li>• Vejakama et al 2017</li> </ul>	QALY	<p>Type: NR</p> <p>Source:</p> <ul style="list-style-type: none"> <li>• Sakthong et al, 2012</li> <li>• Teerawattananon et al, 2007</li> </ul>	3%	3%

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Schlackow, et al <sup>19</sup> UK	<p>Moderate-to-advanced CKD participants</p> <ul style="list-style-type: none"> <li>• <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>): <ul style="list-style-type: none"> <li>• Stage 3b: 30 ≤ eGFR &lt;45</li> <li>• Stage 4: 15 ≤ eGFR &lt;30</li> <li>• Stage 5 not yet receiving renal replacement therapy: &lt;15</li> </ul> </li> <li>• <b>UACR</b> (mg/g): 675 (1196)</li> <li>• <b>ACE/ARB</b>: NR</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type</b>: Markov</li> <li>• <b>Time horizon</b>: Lifetime</li> <li>• <b>Cycle length</b>: 1 year</li> <li>• <b>Perspective</b>: NR</li> </ul>	<p><b>Health states:</b></p> <ul style="list-style-type: none"> <li>• <b>CKD submodel:</b> <ul style="list-style-type: none"> <li>• CKD stages b</li> <li>• CKD stages 4,</li> <li>• CKD stages 5 not on RRT</li> <li>• Dialysis</li> <li>• Kidney transplant</li> </ul> </li> <li>• <b>CVD submodel:</b> <ul style="list-style-type: none"> <li>• Nonvascular death</li> <li>• Vascular death</li> <li>• Nonfatal major atherosclerotic event</li> <li>• Nonfatal haemorrhagic stroke</li> </ul> </li> </ul> <p><b>Adverse events:</b></p> <ul style="list-style-type: none"> <li>• MI</li> <li>• Strokes</li> <li>• Vascular procedures</li> <li>• Hospital admissions</li> <li>• Other serious adverse events</li> </ul>	NR	SHARP trial	QALY	<p><b>Type</b>: Indirect (EQ-5D-3L)</p> <p><b>Source</b>: Study results</p>	NR	NR
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<p>De Vries, et al<sup>30</sup> Netherlands</p>	<p>Patients with CKD stage 4 • <u>eGFR</u> (ml/min/1.73 m<sup>2</sup>): NR • <u>Albuminuria</u>: NR • <u>ACE/ARB</u>: NR</p>	<p>• Type: Markov • Time horizon: NR • Cycle length: NR • Perspective: Health care and societal</p>	<p><u>Health states:</u> • CKD4 conventional treatment • CKD4 prolongation due to new intervention under investigation • ESRD dialysis • ESRD transplantation • Death</p> <p><u>Adverse events:</u> Not included/NR</p>	<p>• One-time cell-based therapy • Biological agents</p>	<p>• OECD: Treatment of Renal Failure (Dialysis and Kidney Transplants), 2011. • Levy et al, 2014 • Hoefield et al, 2010. • Orlando et al 2007</p>	<p>• QALY • Patient benefits from delaying ESRD (Gain in QALY, life expectancy and productive years)</p>	<p>Type: Direct (TTO) Source: • Laupacis et al, 1996 • Gorodetskaya et al, 2005 • Bass et al, 2004 • De Wit GA et al, 1998 • Villa et al, 2012</p>	<p>3%</p>	<p>3%</p>
<p>Mihaylova, et al<sup>31</sup> UK</p>	<p>Patients 40 years or older with CKD but without known coronary heart disease were eligible if they were receiving maintenance dialysis or had serum or plasma creatinine levels of at least 150 mmol/L (1.7 mg/dL) in men or 130 mmol/L (1.5 mg/dL) in women</p>	<p>• Type: No model provided • Time horizon: median follow-up was 4.9 years • Cycle: NR • Perspective: Health care system</p>	<p><u>Health states/events:</u> NA</p> <p><u>Adverse events:</u> • Suspected MI • Stroke, vascular procedure • Cancer • Hospital admission for other reasons • Other serious adverse events</p>	<p>• Simvastatin (20 mg, plus ezetimibe, 10 mg, daily) • Placebo</p>	<p>NR</p>	<p>• Avoiding major atherosclerotic event (MI or death from coronary heart disease, nonhemorrhagic stroke, or arterial revascularization excluding dialysis access procedures) • QALY</p>	<p>Type: NR Source: NR</p>	<p>3.5%</p>	<p>3.5%</p>

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	<ul style="list-style-type: none"> <li>• <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>): <ul style="list-style-type: none"> <li>• Stage 3: ≥30 (83% of participants in this category with CKD stage 3b: 30-45)</li> <li>• Stage 4: 15 to &lt;30</li> <li>• Stage 5: &lt;15</li> </ul> </li> <li>• <b>Albuminuria</b>: NR</li> <li>• <b>ACE/ARB</b>: NR</li> </ul>								
<p>Nguyen, et al<sup>32</sup> Singapore</p>	<p>Incident CKD patients who have not yet started dialysis</p> <ul style="list-style-type: none"> <li>• <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>): NR</li> <li>• <b>Albuminuria</b>: NR</li> <li>• <b>ACE/ARB</b>: NR</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type</b>: Markov</li> <li>• <b>Time horizon</b>: Lifetime</li> <li>• <b>Cycle length</b>: 1 year</li> <li>• <b>Perspective</b>: Third-party payer</li> </ul>	<p><b>Health states</b>:</p> <ul style="list-style-type: none"> <li>• CKD with no dialysis</li> <li>• ESRD</li> <li>• All-cause mortality</li> </ul> <p><b>Adverse events</b>: Not included/NR</p>	<ul style="list-style-type: none"> <li>• Sevelamer</li> <li>• Calcium carbonate</li> </ul>	<ul style="list-style-type: none"> <li>• Literature (mortality risk)</li> <li>• Di Iorio et al, 2012</li> </ul>	QALY	<p>Type: Direct (TTO) Source: Gorodetskaya et al, 2005</p>	3.5%	3.5%
<p>Gandjour, et al<sup>33</sup> Germany</p>	<p>Simulated 65-year-old patients with CKD</p> <ul style="list-style-type: none"> <li>• <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>): Between 75 and 15</li> <li>• <b>Albuminuria</b>: NR</li> <li>• <b>ACE/ARB</b>: example of a DMP</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type</b>: Markov</li> <li>• <b>Time horizon</b>: Lifetime (35 years)</li> <li>• <b>Cycle length</b>: 1 year</li> </ul>	<p><b>Health states</b>:</p> <ul style="list-style-type: none"> <li>• CKD 1 to 4 with no vascular disease</li> <li>• Major vascular disease</li> <li>• ESRD</li> <li>• Death</li> </ul>	<ul style="list-style-type: none"> <li>• DMP</li> <li>• No DMP program</li> </ul>	<ul style="list-style-type: none"> <li>• Mafham et al, 2011</li> <li>• Statistisches Bundesamt, 2013</li> <li>• Frei and Schober-Halstenberg, 2008</li> <li>• Heller et al, 2008</li> </ul>	LYG	<p>Type: NR Source: NR</p>	3%	3%

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	<p><b>component:</b> angiotensin-II– receptor antagonist losartan</p>	<p>• <b>Perspective:</b> Third-party payer</p>	<p><b>Adverse events:</b> Not included/NR</p>		<p>• Gunster et al, 2011 • Icks et al 2011</p>				
<p>Gros, et al <sup>34</sup> Spain</p>	<p>Predialysis and dialysis CKD patients • <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>): NR • <b>Albuminuria:</b> NR • <b>ACE/ARB:</b> NR</p>	<p>• <b>Type:</b> Decision analytical structure and Markov model • <b>Time horizon:</b> Lifetime (35 years) • <b>Cycle length:</b> 1 year • <b>Perspective:</b> Health care system</p>	<p><b>Health states:</b> •Predialysis •Dialysis •Death  <b>Adverse events:</b> Vomiting</p>	<p>• First line CB, second line LC • CBr only • Return to CB</p>	<p>• Levin et al, 2008 • European Dialysis and Transplant Association Registry. 2006. •Kestenbaum et al 2005 • Block et al 2004</p>	<p>• LYG •QALY • Dialysis-free years gained</p>	<p>Type: NR Sources: • Dale et al, 2008 • Nafees et al, 2008</p>	<p>3%</p>	<p>3%</p>
<p>Okubo, et al <sup>35</sup> Japan</p>	<p>Hypothetical cohorts of middle- aged male outpatients with diabetes or CKD • <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>): NR •<b>Albuminuria:</b> NR •<b>ACE/ARB:</b> NR</p>	<p>• <b>Type:</b> Decision analytical structure and Markov model • <b>Time horizon:</b> Lifetime (up to 100 years of age) • <b>Cycle length:</b> 1 year</p>	<p><b>Health states:</b> <b>Diabetes model:</b> • Screened and/or examined diabetes • ESKD • CVD • Amputation • Blindness • Death  <b>CKD model:</b></p>	<p>• Obstructive sleep apnea screening for diabetes or CKD patients • No screening</p>	<p>For diabetes model: • Yokoyama et al, 1997 • Ministry of Health, Labour and Welfare, 2013 • Kondo et al, 2012 • Yokoyama et al, 2012</p>	<p>QALY</p>	<p>Type: NR Sources: • Drummond et al, 2005 • Gold et al, 1996 • Sakamaki et al 2006 • Tajima et al, 2010 • Hisashige et al, 2000 • Saito et al, 2008</p>	<p>3%</p>	<p>3%</p>

eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

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		<ul style="list-style-type: none"> <li>• Perspective: Societal</li> </ul>	<ul style="list-style-type: none"> <li>• Screened and/or examined CKD</li> <li>• ESKD</li> <li>• CVD</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>		<ul style="list-style-type: none"> <li>• Kimura et al, 1998</li> <li>• Fukiyama et al, 2000</li> <li>• The Global Lower Extremity Amputation Study Group, 2000</li> <li>• Izumi et al, 2009</li> <li>• Buchner et al, 2007</li> </ul> <p>For CKD model:</p> <ul style="list-style-type: none"> <li>• Nakayama et al 2010</li> <li>• Ministry of Health, Labour and Welfare, 2013</li> <li>• Buchner et al, 2007</li> <li>• Kondo et al, 2012</li> <li>• Kimura et al, 1998</li> <li>• Fukiyama et al, 2000</li> </ul>		<ul style="list-style-type: none"> <li>• Jenkinson et al, 1997</li> </ul>		
Ruggeri, et al <sup>36</sup> Italy	Adult CKD patients who were new to haemodialysis (<120 days)	• Type: No model provided	NR	<ul style="list-style-type: none"> <li>• Sevelamer</li> <li>• Calcium carbonate</li> <li>• Vitamin D (42% of</li> </ul>	NR	LYG	Type: NR Source: NR	NA	NA

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	<ul style="list-style-type: none"> <li>• eGFR (ml/min/1.73 m<sup>2</sup>): NR</li> <li>• Albuminuria: NR</li> <li>• ACE/ARB: NR</li> </ul>	<ul style="list-style-type: none"> <li>• Time horizon: 3 years</li> <li>• Cycle length: NR</li> <li>• Perspective: Health care system</li> </ul>		<ul style="list-style-type: none"> <li>Sevelamer group and 41% of Calcium group)</li> <li>• Cinacalcet (50% of Sevelamer group and 54% of Calcium group)</li> </ul>					
You, et al <sup>37</sup> Taiwan	<p>Hypothetical cohort of adult CKD patients</p> <ul style="list-style-type: none"> <li>• eGFR (ml/min/1.73 m<sup>2</sup>): <ul style="list-style-type: none"> <li>• Stage 4: 15 – 29</li> <li>• Stage 5: &lt;15</li> </ul> </li> <li>• Albuminuria: NR</li> <li>• ACE/ARB: NR</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: 10 years</li> <li>• Cycle length: 1 month</li> <li>• Perspective: Health care system</li> </ul>	<p><u>Health states:</u></p> <ul style="list-style-type: none"> <li>• CKD stage 4</li> <li>• CKD stage 5</li> <li>• Hemodialysis</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• KA + LPD at CKD 4 (Early initiation)</li> <li>• LPD at CKD stage 4 + initiation of KA supplement at CKD stage 5 (Watchful-waiting group)</li> </ul>	Weng et al, 2014	QALY	<p>Type: NR</p> <p>Source: Gorodetskaya et al, 2005</p>	3%	3%
Levy, et al <sup>38</sup> USA	<p>Population of individuals with pre-ESRD CKD</p> <ul style="list-style-type: none"> <li>• eGFR (ml/min/1.73 m<sup>2</sup>): <ul style="list-style-type: none"> <li>• Stage G3a: ≥45 and &lt;60</li> <li>• Stage G3b: ≥30 and &lt;45</li> <li>• Stage G4: ≥15 and &lt;30</li> <li>• Stage G5: &lt;15</li> </ul> </li> <li>• ESRD: &lt;10</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: Lifetime</li> <li>• Cycle length: 1 year</li> <li>• Perspective: NR</li> </ul>	<p><u>Health states:</u></p> <ul style="list-style-type: none"> <li>• Functioning kidney: eGFR 3a, eGFR 3b, eGFR 4, eGFR 5</li> <li>• ESRD</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• Hypothetical intervention mimicking an effective intervention that slows the rate of eGFR decline</li> <li>• SOC</li> </ul>	<ul style="list-style-type: none"> <li>• Tangri et al, 2011</li> <li>• Hoefield et al, 2010</li> </ul>	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> <li>• Years to ESRD</li> <li>• Number per 1000 reaching ESRD</li> </ul>	<p>Type: Direct (TTO)</p> <p>Sources: <ul style="list-style-type: none"> <li>• Gorodetskaya et al, 2005</li> <li>• Bass et al, 2004</li> <li>• Collins et al 2011</li> </ul> </p>	3	3



eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

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	<ul style="list-style-type: none"> <li>• <b>UACR (mg/g):</b> <ul style="list-style-type: none"> <li>• CKD G 3a: 100</li> <li>• CKD G 3b: 200</li> <li>• CKD G 4: 300</li> <li>• CKD G 5: 350</li> </ul> </li> <li>• <b>ACE/ARB: NR</b></li> </ul>								
Mennini, et al <sup>39</sup> Italy	Patients with CKD stages 4 and 5 • <b>eGFR (ml/min/1.73 m<sup>2</sup>):</b> NR • <b>Albuminuria:</b> NR • <b>ACE/ARB:</b> NR	<ul style="list-style-type: none"> <li>• <b>Type:</b> Markov</li> <li>• <b>Time horizon:</b> 10 years</li> <li>• <b>Cycle length:</b> NR</li> <li>• <b>Perspective:</b> Health care system</li> </ul>	<b>Health states:</b> <ul style="list-style-type: none"> <li>• Death</li> <li>• ESRD</li> <li>• CKD not requiring dialysis</li> </ul> <b>Adverse events:</b> Not included/NR	<ul style="list-style-type: none"> <li>• Very LPD (0.4 g/kg/d)</li> <li>• Moderate LPD (0.7 g/kg/d)</li> </ul>	<ul style="list-style-type: none"> <li>• De Nicola et al, 2010</li> <li>• Cianciaruso et al, 2008</li> <li>• Di Iorio et al, 2003</li> <li>• Ihle et al, 1989</li> <li>• Jungers et al, 1987</li> <li>• Malvy et al, 1999</li> <li>• Mircescu et al, 2007</li> <li>• Williams et al, 1991</li> <li>• Fouque et al, 2009</li> </ul>	QALY	Type: Direct (TTO) Source: Gorodetskaya et al, 2005	3	1.5
Ruggeri, et al <sup>40</sup> Italy	Patients with NDD-CKD • <b>eGFR (ml/min/1.73 m<sup>2</sup>):</b> NR • <b>Albuminuria:</b> NR • <b>ACE/ARB:</b> no significant differences between	<ul style="list-style-type: none"> <li>• <b>Type:</b> No model provided</li> <li>• <b>Time horizon:</b> 3 years</li> <li>• <b>Cycle length:</b> NR</li> </ul>	NR	<ul style="list-style-type: none"> <li>• Sevelamer</li> <li>• Calcium carbonate</li> </ul>	NR	LYG	Type: NR Source: NR	NA	NA

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	treatment groups in the use of ACEi/ARB	• Perspective: Health care system							
Adarkwah, et al <sup>41</sup> Netherlands	<p>Nondiabetic patients with advanced renal insufficiency</p> <ul style="list-style-type: none"> <li>• <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>): Stage 4: 15-26</li> <li>• <b>Albuminuria</b>: NR</li> <li>• <b>ACE/ARB</b>: ACEi (20 mg benazepril daily in base case; 5 mg enalapril daily in the SA)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type</b>: Markov model</li> <li>• <b>Time horizon</b>: Lifetime</li> <li>• <b>Cycle length</b>: 1 year</li> <li>• <b>Perspective</b>: Health care system</li> </ul>	<p><u>Health states</u>:</p> <ul style="list-style-type: none"> <li>• Advanced renal disease (serum creatinine: &gt;3.0 mg/dl, GFR: 15-26 ml/min/1.73 m<sup>2</sup>, CKD stage 4)</li> <li>• ESRD</li> <li>• Death</li> </ul> <p><u>Adverse events</u>: Not included/NR</p>	<ul style="list-style-type: none"> <li>• ACEi</li> <li>• No-treatment</li> </ul>	<ul style="list-style-type: none"> <li>• Ihle et al,1996</li> <li>• Hou et al, 2006</li> <li>• Dutch end-stage renal disease registry</li> <li>• Statline – Central Bureau for Statistics, 2010</li> <li>• Terajima et al, 2003</li> </ul>	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<p><b>Type</b>: Direct (TTO)</p> <p><b>Sources</b>:</p> <ul style="list-style-type: none"> <li>• Hoerger et al, 2010</li> <li>• Churchill et al, 1987</li> <li>• Arnesen et al, 2004</li> </ul>	4%	1.5%
Nasution, et al <sup>42</sup> Indonesia	<p>Patients with CKD stages 4 and 5</p> <ul style="list-style-type: none"> <li>• <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>):</li> <li><b>Control group</b>: <ul style="list-style-type: none"> <li>• CKD stage 4: 14 (17%)</li> <li>• CKD stage 5: 66 (83%)</li> </ul> </li> <li><b>Experimental group</b>: <ul style="list-style-type: none"> <li>• CKD stage 4: 8 (16%)</li> <li>• CKD stage 5: 55 (84%)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type</b>: No model provided</li> <li>• <b>Time horizon</b>: NR</li> <li>• <b>Cycle length</b>: NR</li> <li>• <b>Perspective</b>: Third-party payer</li> </ul>	NR	<ul style="list-style-type: none"> <li>• CPE</li> <li>• No CPE</li> </ul>	NR	Number of lives saved	<p><b>Type</b>: NR</p> <p><b>Source</b>: NR</p>	NR	NR

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	<ul style="list-style-type: none"> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> NR</li> </ul>								
Thompson, et al <sup>43</sup> UK	<p>NDD-CKD patients, ≥18 years old, stage 3-4 CKD</p> <ul style="list-style-type: none"> <li>• <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>): NR</li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> no significant differences between treatment groups</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type:</b> Markov model</li> <li>• <b>Time horizon:</b> Lifetime</li> <li>• <b>Cycle length:</b> 1 month</li> <li>• <b>Perspective:</b> Health care system</li> </ul>	<p><b>Health states:</b></p> <ul style="list-style-type: none"> <li>• CKD not on dialysis</li> <li>• CKD on dialysis</li> <li>• Dead</li> </ul> <p><b>Adverse events:</b> Not included/NR</p>	<ul style="list-style-type: none"> <li>• Sevelamer (1600 mg/day)</li> <li>• Calcium carbonate (2000 mg/day)</li> </ul>	INDEPENDENT-CKD study (Di Iorio et al, 2012)	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<p><b>Type:</b> Direct (HUI-3 and TTO)</p> <p><b>Source:</b> Gorodetskaya et al, 2005</p>	3.5%	3.5%
Wiebe, et al <sup>44</sup> Canada	<p>CKD patients (stage 3b-4) currently residing further than a &gt;120-minute drive from a nephrology clinic</p> <ul style="list-style-type: none"> <li>• <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>): Stages 3b-4: &lt;45</li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> Authors assumed that adding a clinic (ie., reducing the distance to the closest nephrologist for simulated patients) would lead to a higher</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type:</b> Markov</li> <li>• <b>Time horizon:</b> Lifetime</li> <li>• <b>Cycle length:</b> 6 months</li> <li>• <b>Perspective:</b> Public payer’s perspective</li> </ul>	<p><b>Health states:</b></p> <ul style="list-style-type: none"> <li>• Alive with stage 3b-4 CKD, distance &gt;120 min</li> <li>• Alive with stage 3b-4 CKD, distance 60.1-120 min</li> <li>• Alive with stage 3b-4 CKD, distance 30.1-60 min</li> <li>• Alive with stage 3b-4 CKD, distance ≤ 30 min</li> <li>• Dialysis</li> </ul>	<ul style="list-style-type: none"> <li>• New clinic formation across driving distance categories: <ul style="list-style-type: none"> <li>• ≤30 min</li> <li>• 30.1–60 min</li> <li>• 60.1–120 min</li> <li>• SOC: &gt;120 min</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Manns et al, 2010</li> <li>• Canadian Organ Replacement Registry</li> <li>• Assumptions</li> <li>• Statistics Canada</li> </ul>	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<p><b>Type:</b> Direct/indirect (EQ-5D and TTO)</p> <p><b>Source:</b></p> <ul style="list-style-type: none"> <li>• Gorodetskaya et al, 2005</li> <li>• Laupacis et al, 1996</li> <li>• Manns et al, 2003</li> </ul>	5%	5%

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	likelihood of the use of statins and ACEi or ARBs		<ul style="list-style-type: none"> <li>• Transplantation</li> <li>• Dead</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>						
Hopkins, et al <sup>45</sup> Canada	<p>Patients with CKD</p> <ul style="list-style-type: none"> <li>• <u>eGFR</u> (ml/min/1.73 m<sup>2</sup>): Stage 3/4: 42</li> <li>• <u>Proteinuria</u>: &gt; 1 g/d existed in 19 patients in total (6 intervention and 13 control).</li> <li>• <u>ACE/ARB</u>: Use of ACEi or ARB with dose increased to achieve BP target and minimize proteinuria</li> </ul>	<ul style="list-style-type: none"> <li>• Type: No model provided</li> <li>• Time horizon: 2 years</li> <li>• Cycle length: NR</li> <li>• Perspective: Payer or societal perspective</li> </ul>	NA	<ul style="list-style-type: none"> <li>• Chronic disease management consisting of the following:                             <ul style="list-style-type: none"> <li>- Achievement of BP target (&lt;130/80)</li> <li>- Use of ACEi or ARB with dose increased to achieve BP target and minimize proteinuria</li> <li>- Management of dyslipidemia primarily by statin (target LDL &lt;2.6 mmol/L)</li> <li>- Treatment of renal anaemia by erythropoietic drugs (target Hb 105 to 120 g/L) and iron as indicated</li> <li>- Use of diet,</li> </ul> </li> </ul>	NA	QALY	<p>Type: Indirect (HUI-3) Source: CanPREVENT</p>	5%	5%

eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

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				<p><b>phosphate binders, and activated vitamin D to maintain serum phosphate, calcium, and parathyroid hormone in target range</b></p> <ul style="list-style-type: none"> <li>- Use of antiplatelet therapy if cardiovascular disease or diabetes</li> <li>- <math>\beta</math>-Blockade with dose titration if post MI or heart failure;</li> <li>- Efforts to help smoking cessation</li> <li>- Diabetes control with target Hba1c&lt;7%;</li> <li>- Metabolic acidosis control;</li> <li>- Diet appropriate to the medical condition.</li> </ul> <p>• SOC</p>					
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<p>Orlando, et al<sup>46</sup> USA</p>	<p>US CKD static population • <u>eGFR</u> (ml/min/1.73 m<sup>2</sup>): Stages 1-5 CKD • <u>Proteinuria</u>: • CKD Stage 1: 14.3% • CKD Stage 2: 14.3% • CKD Stage 3: 6.1% • CKD Stage 4: 42.6% • CKD Stage 5: NA • <u>ACE/ARB</u>: NR</p>	<p>• Type: Markov • Time horizon: Lifetime • Cycle length: 1 month • Perspective: NR</p>	<p><u>Health states</u>: • CKD stages 1-5 • Dialysis • Bone disease • MI • CHF • Stroke without disability • Stroke with disability • Fistula placement • Transplantation • Death  <u>Adverse events</u>: Not included/NR</p>	<p>• Treatment with an ACEi • Treatment with an HMG-CoA reductase inhibitor • Management by a nephrologist • Control of diabetes • Control of hypertension • Calcium and phosphorous management • Implementation of a CKD screening program</p>	<p>• Coresh et al, 2003 • Keith et al, 2004 • Perneger et al, 1993 • Tonelli et al, 2004</p>	<p>QALY</p>	<p>Type: NR Source: • Opinion • Mittman et al, 1996 • Shephard et al, 1998 • Post et al, 2001 • National Diabetes Surveillance System • Geiss et al, 2002</p>	<p>NA</p>	<p>3% (utilities)</p>
<p>Vegter, et al<sup>47</sup> UK</p>	<p>Predialysis CKD population and Incident dialysis population • <u>eGFR</u> (ml/min/1.73 m<sup>2</sup>): NR • <u>Albuminuria</u>: NR • <u>ACE/ARB</u>: NR</p>	<p>• Type: Decision analytical structure and Markov model • Time horizon: Lifetime (40 years) • Cycle length: 1 year</p>	<p><u>Health states</u>: • Predialysis patients • Dialysis patients • Death  <u>Adverse events</u>: Vomiting</p>	<p>• First line CB, second line LC • CB only • Return to CB</p>	<p>• Keith et al, 2004 • US Renal Data System, 2010 • Levin et al, 2008 • Block et al, 2004 • Kestenbaum et al, 2005</p>	<p>• LYG • QALY • Dialysis-free years gained</p>	<p>Type: NR Source: • Davison et al, 2008 • Gorodetskaya et al, 2005 • Osoba et al, 1997 • Dale et al, 2008</p>	<p>3.5%</p>	<p>3.5%</p>

eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

From a supplement to *The American Journal of Managed Care*<sup>®</sup>: “Patients With Diabetes and Chronic Kidney Disease: ACE Inhibitor or ARB Treatment, Medical Costs for Disease Management, and the FINE-CKD Model to Evaluate Economic Value of Finerenone”

		<ul style="list-style-type: none"> <li>• Perspective: Health care system</li> </ul>							
Black, et al <sup>17</sup> UK	<p>A cohort of individuals with non-diabetic CKD</p> <ul style="list-style-type: none"> <li>• <b>eGFR</b> (ml/min/1.73 m<sup>2</sup>): 15–59</li> <li>• <b>Albuminuria</b>: <ul style="list-style-type: none"> <li>• ACR &lt; 30 mg/g</li> <li>• ACR ≥ 30 mg/g</li> </ul> </li> <li>• <b>ACE/ARB</b>: Costs of ACEi or ARB were used in the model</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: 35 years</li> <li>• Cycle length: NR</li> <li>• Perspective: Health care system</li> </ul>	<p><b>Health states:</b></p> <ul style="list-style-type: none"> <li>• CKD 1 and 2 combined to form a single state (eGFR ≥ 60 ml/min/1.73 m<sup>2</sup>) <ul style="list-style-type: none"> <li>-with MA</li> <li>-with proteinuria</li> <li>-with MA/CVD</li> <li>-with proteinuria/CVD</li> </ul> </li> <li>• CKD 3a (eGFR 45–59 ml/min/1.73 m<sup>2</sup>) <ul style="list-style-type: none"> <li>-with MA</li> <li>-with proteinuria</li> <li>-with CVD</li> <li>-with MA/CVD</li> <li>-with proteinuria/CVD</li> </ul> </li> <li>• CKD 3b (eGFR 30–44 ml/min/1.73 m<sup>2</sup>) <ul style="list-style-type: none"> <li>-with MA</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Early referral strategy</li> <li>• Standard practice (Referral upon transit to stage 5 CKD)</li> </ul>	<ul style="list-style-type: none"> <li>• Hallan et al, 2007</li> <li>• Primary Care Clinical Informatics Unit research database</li> </ul>	QALY	<p>Type: Indirect (HUI-3)</p> <p>Source: Gorodetskaya et al, 2005</p>	3.5%	3.5%

eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

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			<ul style="list-style-type: none"> <li>-with proteinuria</li> <li>-with CVD</li> <li>-with MA/CVD</li> <li>-with proteinuria/CVD</li> <li>• CKD 4</li> <li>-with MA</li> <li>-with proteinuria</li> <li>-with CVD</li> <li>-with MA/CVD</li> <li>-with proteinuria/CVD</li> <li>• ESRD</li> <li>• Death</li> <li>-from other causes</li> <li>-from CVD</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>						
Hoerger, et al <sup>22</sup> USA	<p>Patients with CKD</p> <ul style="list-style-type: none"> <li>• <u>eGFR</u> (ml/min/1.73 m<sup>2</sup>): 101.9 (19.3)</li> <li>• <u>Albuminuria:</u> <ul style="list-style-type: none"> <li>• Persistent microalbuminuria (sustained ACR of 30- 299 mg/g)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Type: Discrete state simulation</li> <li>• Time horizon: Lifetime</li> <li>• Cycle length: NR</li> </ul>	<p><u>Health states:</u></p> <ul style="list-style-type: none"> <li>• No CKD</li> <li>• CKD stages 1-5</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• Usual care, including incidental screening for persons with diabetes or hypertension</li> </ul>	<ul style="list-style-type: none"> <li>• NHANES data</li> <li>• Adler et al, 2003</li> </ul>	QALY	<p>Type: Direct (TTO) (GFR values)</p> <p>Sources:</p> <ul style="list-style-type: none"> <li>• Assumption</li> <li>• Boulware et al 2003</li> </ul>	3%	3%



eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

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	<ul style="list-style-type: none"> <li>• <b>Macroalbuminuria (ACR ≥ 300 mg/g)</b></li> <li>• <b>ACE/ARB:</b> The primary analysis simulates screening for micro- and macroalbuminuria followed by treatment with ACE inhibitors or ARBs</li> <li>• Depending on the presence of diabetes and hypertension, each person with microalbuminuria received either ACEi (hypertension or neither) or ARBs (diabetes).</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Perspective:</b> Health care system</li> </ul>		<ul style="list-style-type: none"> <li>• ACEi</li> <li>• ARBs</li> </ul>			<ul style="list-style-type: none"> <li>• <b>Gorodetskaya et al, 2005</b></li> </ul>		
Sabariago, et al <sup>48</sup> Germany	<p>CKD patients who received an inpatient renal rehabilitation program developed at the Sinnatal Clinic</p> <ul style="list-style-type: none"> <li>• <b>eGFR (ml/min/1.73 m<sup>2</sup>):</b> NR</li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> NR</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type:</b> No model provided</li> <li>• <b>Time horizon:</b> 12 months</li> <li>• <b>Cycle length:</b> NR</li> <li>• <b>Perspective:</b> Societal</li> </ul>	NR	<ul style="list-style-type: none"> <li>• <b>Multidisciplinary educational program</b></li> <li>• <b>Standard educational program</b></li> </ul>	NR	Mean calendar days in the workforce within the first year after discharge	Type: NR Source: NR	NA	NA

eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

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Scalone, et al <sup>49</sup> Germany	Elderly nondiabetic CKD5 patients • <u>eGFR</u> (ml/min/1.73 m <sup>2</sup> ): Stage 5 CKD • <u>Albuminuria</u> : NR • <u>ACE/ARB</u> : NR	• Type: CBA • Time horizon: NR • Cycle length: NR • Perspective: Health care system	NR	• Supplemented very LPD • Dialysis	NR	None	Type: NR Source: NR	5%	5%
Vegter, et al <sup>50</sup> Netherlands	Patients with non-diabetic nephropathy • <u>eGFR</u> (ml/min/1.73 m <sup>2</sup> ): NR • <u>Albuminuria</u> : NR • <u>ACE/ARB</u> : ACEi (ramipril)	• Type: Decision analytical structure and Markov model • Time horizon: 10 years • Cycle length: 1 month • Perspective: Third-party payer	<u>Health states</u> : • CKD • ESRD • Death  <u>Adverse events</u> : Not included/NR	<i>First study objective</i> : • ACEi (ramipril) • Placebo <i>Second study objective</i> : • Selective screen of the ACE (I/D) genotype-and-treat strategy • No screening	• GISEN Group, 1997 • Ruggenenti et al, 2005 • Dutch End-Stage Renal Disease Registry	QALY	Type: Indirect (HUI-3) Source: Gorodetskaya et al, 2005	3%	3%
Takahashi, et al <sup>51</sup> Japan	Nondiabetic CKD patients with elevated serum creatinine • <u>eGFR</u> (ml/min/1.73 m <sup>2</sup> ): NR • <u>Albuminuria</u> : NR • <u>ACE/ARB</u> : NR	• Type: Markov model • Time horizon: 3 years • Cycle length: 3 months	<u>Health states</u> : • Serum creatinine (sCr) 5.0 mg/dL • sCr 6.0 mg/dL • sCr 7.0 mg/dL • sCr 8.0-11.9 mg/dL • Hemodialysis	• AST-120 • Placebo	Koide et al, 1987	QALY	Type: NR Sources: • Hogan et al, 2002 • Smith et al, 2004	3%	3%

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		<ul style="list-style-type: none"> <li>• Perspective: Japanese reimbursement perspective</li> </ul>	<ul style="list-style-type: none"> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>						
Gal-Moscovici and Sprague <sup>52</sup> USA	<p>Patients with CKD stage 4</p> <ul style="list-style-type: none"> <li>• eGFR (ml/min/1.73 m<sup>2</sup>): NR</li> <li>• Albuminuria: NR</li> <li>• ACE/ARB: NR</li> </ul>	<ul style="list-style-type: none"> <li>• Type: CBA</li> <li>• Time horizon: NR</li> <li>• Cycle length: NR</li> <li>• Perspective: Health care payer</li> </ul>	NR	<ul style="list-style-type: none"> <li>• Paricalcitol</li> <li>• Calcitriol</li> </ul>	NR	<ul style="list-style-type: none"> <li>• Rate of all-cause hospitalization</li> <li>• Number of all-Cause hospital days</li> </ul>	Type: NR Source: NR	NR	NR
Van Hout, et al <sup>53</sup> Netherlands	<p>Patients with chronic renal insufficiency</p> <ul style="list-style-type: none"> <li>• eGFR (ml/min/1.73 m<sup>2</sup>): NR</li> <li>• Albuminuria: NR</li> <li>• ACE/ARB: ACEi (Benazepril)</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Semi-Markov</li> <li>• Time horizon: <ul style="list-style-type: none"> <li>• 3 years</li> <li>• 10 years</li> </ul> </li> <li>• Cycle length: 3 months</li> <li>• Perspective: NR</li> </ul>	<p><u>Health states:</u></p> <ul style="list-style-type: none"> <li>• Chronic renal insufficiency</li> <li>• Hemodialysis</li> <li>• Post transplantation</li> <li>• Second haemodialysis (after graft rejection)</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• Benazepril</li> <li>• Placebo</li> </ul>	<ul style="list-style-type: none"> <li>• AIPRI trial</li> <li>• RENINE</li> </ul>	<ul style="list-style-type: none"> <li>• LYG</li> <li>• Surviving</li> <li>• Surviving without ESRD</li> </ul>	Type: NR Source: NR	5%	5%

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<p>Ludbrook<sup>54</sup> UK</p>	<p>Patients with chronic renal insufficiency</p> <ul style="list-style-type: none"> <li>• <u>eGFR</u> (ml/min/1.73 m<sup>2</sup>): NR</li> <li>• <u>Albuminuria</u>: NR</li> <li>• <u>ACE/ARB</u>: NR</li> </ul>	<ul style="list-style-type: none"> <li>• <u>Type</u>: Markov</li> <li>• <u>Time horizon</u>: NR</li> <li>• <u>Cycle length</u>: 1 month</li> <li>• <u>Perspective</u>: NR</li> </ul>	<p><u>29 health states</u>:</p> <ul style="list-style-type: none"> <li>• 1 to 6: Dialysis training period</li> <li>• 7: Hospital dialysis</li> <li>• 8: Home dialysis</li> <li>• 9 to 15: First transplant</li> <li>• 16: Rejection</li> <li>• 17: Hospital dialysis</li> <li>• 18: Home dialysis</li> <li>• 19 to 25: Second transplant</li> <li>• 26: Rejection</li> <li>• 27: Hospital dialysis</li> <li>• 28: Home dialysis</li> <li>• 29: Death</li> </ul> <p><u>Adverse events</u>: Not included/NR</p>	<ul style="list-style-type: none"> <li>• <u>Treatment 1</u>: Hospital dialysis alone</li> <li>• <u>Treatment 2</u>: Home dialysis and periodic hospital dialysis</li> <li>• <u>Treatment 3</u>: Hospital dialysis, home dialysis and transplantation</li> </ul>	<ul style="list-style-type: none"> <li>• Shah and Foot, 1978</li> <li>• European Dialysis and Transplant Association, 1976</li> <li>• Assumptions</li> </ul>	<p>LYG</p>	<p><u>Type</u>: NR <u>Source</u>: NR</p>	<ul style="list-style-type: none"> <li>• 7%</li> <li>• 15%</li> </ul>	<p>NR</p>
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HMGCo-A, 3-Hydroxy-3-methylglutaryl-coenzyme A.

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**eAppendix Table 4.** Overview of Cost-effectiveness Models Among CKD Patients With Other Diseases

Author, year, country	Study population (eg eGFR, albuminuria, ACE/ARB)	Model summary (type, time horizon, cycle length, perspective)	Health states /events and adverse events list	Treatment arms	Transition probability sources	Efficacy measures	Utility types and source	Disco unt rate for cost	Disco unt rate for effect
Javanbakht, et al <sup>55</sup> UK	Hypothetical cohort of patients with CKD stage 3–4 undergoing DAG and/or PCI • <u>eGFR</u> : 15–60 ml/min/1.73 m <sup>2</sup> • <u>Albuminuria</u> : NR • <u>ACE/ARB</u> : NR	<ul style="list-style-type: none"> <li>• Type: Decision analytical structure and Markov model</li> <li>• Time horizon: - Decision tree: 3 months - Markov: Lifetime</li> <li>• Cycle: 3 months</li> <li>• Perspective: NHS and PSS</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• CKD 3-4</li> <li>• CI-AKI</li> <li>• CKD 5</li> <li>• CKD 3-4 (AKI history)</li> <li>• MI (CKD 3-4)</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• DyeVert PLUS EZ System</li> <li>• Current practice without the use of the DyeVert PLUS EZ system</li> </ul>	<ul style="list-style-type: none"> <li>• Dangas et al 2005</li> <li>• Fahy et al 2004</li> <li>• Eriksen et al 2006</li> <li>• James et al 2010</li> <li>• Shah et al 2019.</li> <li>• NICE CG169. 2013. Accessed Aug 2019.</li> <li>• Valle et al 2017</li> </ul>	QALY	<p><u>Type:</u> Indirect (EQ-5D)</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Tajima et al 2010</li> <li>• Kindet al 1998</li> <li>• Sullivan et al 2011</li> <li>• Assumption</li> </ul>	3.5%	3.5%
Kalantar-Zadeh, et al <sup>56</sup> USA	Hypothetical cohort of patients with CKD stages 3–4 that have SHPT, and VDI	<ul style="list-style-type: none"> <li>• Type: Decision analytical structure</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• CKD stage steady</li> <li>• CKD stage progression</li> <li>• Death</li> </ul>	<ul style="list-style-type: none"> <li>• ERC</li> <li>• Paricalcitol</li> </ul>	<ul style="list-style-type: none"> <li>• Anwar et al 2014.</li> <li>• Lishmanov et al 2012</li> <li>• West et al 2015</li> <li>• Li et al 2015</li> </ul>	<ul style="list-style-type: none"> <li>• QALY</li> <li>• LYG</li> <li>• CV events</li> <li>• Fractures events</li> </ul>	<p><u>Type:</u> Direct (TTO)</p> <p><u>Sources:</u></p>	3%	3%

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	<ul style="list-style-type: none"> <li>• <b>eGFR:</b> stages 3–4 according to KDIGO classification</li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> NR</li> </ul>	<p>and Markov model</p> <ul style="list-style-type: none"> <li>• Time horizon: 5 years</li> <li>• Cycle: 1 year</li> <li>• Perspective: Third-party payer</li> </ul>	<p><u>Adverse events:</u></p> <ul style="list-style-type: none"> <li>• Cardiovascular events</li> <li>• Fracture events</li> <li>• CKD stage progression</li> <li>• Other adverse events</li> </ul>			<ul style="list-style-type: none"> <li>• Number of patient-years in stage 5</li> <li>• Deaths averted/patients alive at end of analysis</li> </ul>	<ul style="list-style-type: none"> <li>• Lee et al 2013</li> <li>• USRDS 2017 annual report v1, CH 6 health expenditures for persons with CKD</li> </ul>		
SMC <sup>57</sup> Scotland	<p>Patients with HK (defined as a serum potassium of &gt;6.0mmol/L) with CKD stage 3b to 5 and/or HF, who would otherwise need to down-titrate or discontinue their RAASi therapy to maintain a clinically acceptable serum potassium level (normocalcemia)</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> NR</li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> RAASi therapy</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Patient-level simulation model</li> <li>• Time horizon: Lifetime (80 years)</li> <li>• Cycle: NR</li> <li>• Perspective: Health care system**</li> </ul>	<p><u>Health states/events:</u></p> <p>The model structure covered a broad range of health states relating to the underlying disease (Heart failure: New York Heart Association I–IV; CKD: CKD3b – CKD5), treatment-related factors (RAASi changes, treatment-related adverse events and treatment initiation/discontinuation), adverse clinical outcomes (HK events [“severe” or “less severe,” CV events, hospitalization) and a number of absorbing health states (background mortality HF mortality, CKD mortality and receipt of renal replacement therapy)</p>	<ul style="list-style-type: none"> <li>• Sodium zirconium cyclosilicate</li> <li>• SOC: The choice of comparator differed depending on the severity of the HK, with patients experiencing a serum potassium level of <math>\geq 6.5</math>mmol/L receiving emergency insulin-dextrose, and the remaining patients receiving dietary intervention and</li> </ul>	<ul style="list-style-type: none"> <li>• Three phase III studies: ZS-003, ZS-004 and ZS-005</li> <li>• Published literature sources</li> </ul>	QALY	<p><u>Type:</u> NR</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Göhler et al 2009</li> <li>• Eriksson et al 2016</li> </ul>	NR	NR

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			<u>Adverse events:</u> Treatment-related adverse events	modification of concomitant medications such as RAASi					
SMC <sup>58</sup> Scotland	Adult patients with CKD stage 3 or 4 with or without HF, with a serum potassium level of >6.0mmol/L who are receiving or RAASi • <u>eGFR</u> : ≥15 to <60 ml/min/1.73 m <sup>2</sup> • <u>Albuminuria</u> : NR • <u>ACE/ARB</u> : RAASi therapy	• <u>Type</u> : Markov • <u>Time horizon</u> : Lifetime (35 years) • <u>Cycle</u> : 1 month • <u>Perspective</u> : NHS and Social Care	<u>Health states/events</u> : Health states were defined by a combination of CKD stage, CV event status and serum potassium levels.  <u>Adverse events</u> : Treatment-related adverse events	• Patiromer (8.4g /day in patients with mild HK and 16.8g /day with moderate to severe HK) and a stable dose of at least 1 RAASi: • SOC dietary modification and RAASi dose modification	• OPAL-HK • CPRD	QALY	<u>Type</u> : Indirect (EQ-5D)**  <u>Sources</u> : • Jones et al 2016 • Jesky et al 2016 • Pockett et al 2018	NR	NR
Snyder, et al <sup>59</sup> USA	Hypothetical cohort of 1000 stage 3 or 4 CKD patients with VDI, and SHPT not on dialysis aged 65 and older • <u>eGFR</u> : NR • <u>Albuminuria</u> : NR • <u>ACE/ARB</u> : NR	• <u>Type</u> : Markov • <u>Time horizon</u> : 5 years • <u>Cycle</u> : 1 year • <u>Perspective</u> : Third-party payer	<u>Health states/events</u> : • CKD stage steady • CKD stage progression • Death  <u>Adverse events</u> : • Any CV events • Any fracture • Mortality • Hypercalcemia	• Vitamin D treatment in CKD stages 3 and 4 • No treatment or delayed treatment with vitamin D in stage 5/ESRD	Anwar and Mahmoud 2014	• QALY • CV events averted • Fractures averted • Time in CKD stage 5/ESRD • LYG	<u>Type</u> : Direct (TTO)  <u>Sources</u> : • Gorodetskaya et al 2005 • Davies et al 2015	3%	3%
Widen, et al <sup>60</sup> Sweden	Patients with stage 3–4 CKD and HK taking RAASi	• <u>Type</u> : Markov	<u>Health states/events</u> : • CKD stages 3–4 with mild HK	• Patiromer: either 8.4-g sachet or 16.8-g	• OPAL-HK trial • Xie et al 2016 • Smith et al 2011.	• LYG • QALY	<u>Type</u> : Indirect (EQ-5D)	3%	3%

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	<ul style="list-style-type: none"> <li>• <b>eGFR*</b>: 36.8 (16.1) ml/min/1.73 m<sup>2</sup></li> <li>• <b>Albuminuria</b>: NR</li> <li>• <b>ACE/ARB*</b>: Initial treatment phase (part A); patiromer group (n = 131): n (%) <ul style="list-style-type: none"> <li>- ACEi: 90 (68.7)</li> <li>- ARB 48 (36.6)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Time horizon</b>: Lifetime (28 years)</li> <li>• <b>Cycle</b>: 1 month</li> <li>• <b>Perspective</b>: Health care system</li> </ul>	<ul style="list-style-type: none"> <li>• <b>CKD progression ESRD</b></li> <li>• <b>HK</b></li> <li>• <b>CV event (MI/stroke)</b></li> <li>• <b>Post-CV event (CKD stages 3-4 with mild HK)</b></li> <li>• <b>Death</b></li> </ul> <p><u>Adverse events:</u></p> <ul style="list-style-type: none"> <li>• <b>CKD progression—MRSA</b></li> <li>• <b>Patiromer—constipation</b></li> <li>• <b>Patiromer—diarrhoea</b></li> <li>• <b>Patiromer—nausea</b></li> </ul>	<ul style="list-style-type: none"> <li>• sachet per diem in combination with RAASi</li> <li>• No patiromer</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Statistics Sweden</b> Accessed 05 Dec 2016.</li> <li>• Landray et al 2010.</li> <li>• Morel et al 2011</li> <li>• Ariyaratne et al 2013</li> <li>• Luo et al 2016.</li> <li>• Tuso 2013</li> </ul>		<p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Wyld et al 2012</li> <li>• Thokala et al 2013.</li> <li>• Taylor et al 2009.</li> <li>• Liem et al 2008</li> <li>• Jones-Hughes et al 2016.</li> <li>• Ara and Brazier 2010</li> <li>• Health Survey for England: Craig et al 2012. Accessed 24 Sep 2018</li> <li>• Wald et al 2000</li> </ul>		
NICE <sup>61</sup> UK	<ul style="list-style-type: none"> <li>• Patients with stage 3-4 CKD and HF comorbidity (CKD HF+) with a serum potassium of ≥5.5 mmol/L at baseline</li> <li>• Patients with stage 3-4 CKD without HF comorbidity (CKD</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type</b>: Markov</li> <li>• <b>Time horizon</b>: Lifetime (35 years)</li> <li>• <b>Cycle</b>: 1 month</li> <li>• <b>Perspective</b>:</li> </ul>	<p><u>Health states/events:</u></p> <p>Model includes CKD stage 3 and 4 health states which are further stratified by serum K+ category and an ESRD stage. From any of these health states patients may experience a CV event or death</p>	<ul style="list-style-type: none"> <li>• <b>Patiromer</b>: 8.4 – 16.8g</li> <li>• <b>SOC</b> (ie., dietary modification and RAASi dose modification)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>OPAL-HK trial</b></li> <li>• CPRD</li> <li>• Xie et al 2016</li> </ul>	QALY	<p><u>Type:</u></p> <p>NR</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• NICE Single Technology Appraisal [ID1293]</li> <li>• Weir et al 2015</li> </ul>	3.5%	3.5%



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	[no HF]) with a serum potassium level of >6.0 mmol/L <ul style="list-style-type: none"> <li>• eGFR: NR</li> <li>• <u>Albuminuria</u>: NR</li> <li>• <u>ACE/ARB</u>: All patients were on at least 1 RAASi (the majority using ACE inhibitors, followed by ARBs and a small proportion on aldosterone antagonists)</li> </ul>	NHS and PSS	<u>Adverse events</u> : <ul style="list-style-type: none"> <li>• Constipation</li> <li>• Diarrhoea</li> <li>• Nausea</li> <li>• Hypomagnesemia</li> </ul>				<ul style="list-style-type: none"> <li>• Kerr et al 2012</li> <li>• Assumption</li> <li>• Jesky et al 2016</li> <li>• Pockett et al 2018</li> <li>• Jones-Hughes et al 2016.</li> <li>• Sullivan et al 2011</li> <li>• Kristiansen et al (999</li> <li>• Nafees et al 2008</li> </ul>		
Goh, et al Malaysia <sup>62</sup>	Patients with CKD not on dialysis with hyperphosphatemia <ul style="list-style-type: none"> <li>• eGFR: NR</li> <li>• <u>Albuminuria</u>: NR</li> <li>• <u>ACE/ARB</u>: NR</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: Lifetime (60 years)</li> <li>• Cycle: 1 year</li> <li>• Perspective: Third-party payer</li> </ul>	<u>Health states/events</u> : <ul style="list-style-type: none"> <li>• CKD not on dialysis</li> <li>• CKD on dialysis</li> <li>• Death</li> </ul> <u>Adverse events</u> : Not included/NR	<ul style="list-style-type: none"> <li>• Sevelamer</li> <li>• Calcium carbonate (CaCO3)</li> </ul>	The INDEPENDENT-CKD trial: Di Iorio, et al 2012	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<u>Type</u> : NR <u>Sources</u> <ul style="list-style-type: none"> <li>• Gorodetskaya, et al 2005.</li> <li>• Bavanandanet al 2010:</li> </ul>	3%	3%
SMC <sup>63</sup> Scotland	Patients with stage 3 or 4 CKD on stable doses of at least 1 RAASi	<ul style="list-style-type: none"> <li>• Type: Markov</li> </ul>	<u>Health states/events</u> : <ul style="list-style-type: none"> <li>• CKD stages 3-4</li> <li>• Stage 5 CKD or ESRD</li> </ul>	<ul style="list-style-type: none"> <li>• Patiromer: 8.4g / day in patients with potassium concentration 5.1</li> </ul>	<ul style="list-style-type: none"> <li>• Published sources</li> <li>• OPAL-HK</li> </ul>	QALY	<u>Type</u> : Direct/indirect (various,	NR	NR

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	<p>treatment who develop HK</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> ≥15 to &lt;60 ml/min/1.73 m<sup>2</sup></li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB*:</b> stable dose of at least 1 RAASi; RAASi were still used by 94% and 44% of patiromer-treated patients and placebo patients, respectively, at the end of the withdrawal phase. At the start of the withdrawal phase, 38% of patiromer patients and 40% of placebo patients were judged to be on maximal dose RAASi.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Time horizon:</b> 35 years</li> <li>• <b>Cycle:</b> 1 month</li> <li>• <b>Perspective:</b> Health care system**</li> </ul>	<ul style="list-style-type: none"> <li>• <b>HK (serum potassium ≥5.5mmol/L) resulting in hospitalization</b></li> <li>• <b>CV event (MI or stroke)</b></li> <li>• <b>post-CV event, or straight to the CV event state</b></li> <li>• <b>Death</b></li> </ul> <p><u>Adverse events:</u> Included, but not specified</p>	<p>to &lt;5.5mmol/L, and 16.8g / day in those with potassium concentration ≥5.5 to &lt;6.5mmol/L.</p> <ul style="list-style-type: none"> <li>• <b>The comparator in the economic analysis was not clearly specified</b></li> <li>• <b>In both treatment arms patients could continue to receive RAASi treatment</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Meta-analysis of RCTs:</b> Xie et al 2016</li> <li>• <b>CPRD</b></li> </ul>	<p>including EQ-5D)</p> <p><u>Sources:</u> Published sources</p>			
<p>Elbasha, et al<sup>64</sup> USA</p>	<p>Treatment-naïve and treatment-experienced patients with hepatitis C virus genotype 1 infection and CKD</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> Stages 1-5 according to</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type:</b> Semi-Markov</li> <li>• <b>Time horizon:</b> Lifetime</li> <li>• <b>Cycle:</b> 1 year</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• CKD1</li> <li>• CKD2</li> <li>• CKD3a</li> <li>• CKD3b</li> <li>• CKD4</li> <li>• CKD 5</li> <li>• HD</li> </ul>	<ul style="list-style-type: none"> <li>• Elbasvir/ grazoprevir</li> <li>• Peg-IFN/RBV</li> </ul>	<ul style="list-style-type: none"> <li>• Weinstein et al 2010</li> <li>• Liu et al 2010.</li> <li>• Nuijten et al 2009</li> <li>• Boulware et al 2003</li> </ul>	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<p><u>Type:</u> NR</p> <p><u>Sources:</u> • Park et al 2015</p> <ul style="list-style-type: none"> <li>• Gorodetskaya et al 2005</li> </ul>	NR	NR

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	<b>KDIGO classification</b> • <b>Albuminuria: NR</b> • <b>ACE/ARB: NR</b>	• <b>Perspective: Third-party payer</b>	• <b>Kidney transplantation</b>  <b>Adverse events: Not included/NR</b>				• <b>Hogan et al 2002</b>		
NICE <sup>65</sup> UK	ADPKD in adults with CKD stages 1 to 3 at initiation of treatment • <b>eGFR:</b> - Average: 82 ml/min/1.73 m <sup>2</sup> - Stages 2-3b according do KDIGO classification • <b>Albuminuria: NR</b> • <b>ACE/ARB: NR</b>	• <b>Type: Patient-level simulation model</b> • <b>Time horizon: Lifetime (80 years)</b> • <b>Cycle: 1 year</b> • <b>Perspective: NHS and PSS</b>	<b>Health states/events:</b> • <b>The ADPKD module:</b> - CKD stages 1 to 4 - A significant pain health state - Death • <b>The ESRD module:</b> - CKD stage 5 - Conservative care - HD - PD - Transplant - Death  <b>Adverse events:</b> Clinically significant pain	• <b>Tolvaptan: twice daily (up to a maximum total daily dose of 120 mg):</b> The dose was titrated at weekly intervals over a 3-week period, initially administered at doses of 45 mg and 15 mg, in the morning and afternoon respectively, and titrated to 60 mg and 30 mg, and then to 90 mg and 30 mg, according to patient-reported tolerability. Following the titration period, patients had the maximum tolerated dose for the remainder of the 36-month treatment period.	TEMPO 3:4 trial	QALY	<b>Type:</b> Direct/indirect (TTO/EQ-5D)  <b>Sources:</b> • Gorodetskaya et al 2005 • Lee et al 2005 • Dolan et al 1997	3.5%	3.5%

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				• SOC					
SMC <sup>66</sup> Scotland	ADPKD in adults with CKD stages 1 to 3 at initiation of treatment • <u>eGFR</u> : NR • <u>Albuminuria</u> *: Worsening albuminuria - Tolvaptan: 961 (100) - Placebo: 483 (99.7) • <u>ACE/ARB</u> : NR	• Type: Patient-level simulation model • Time horizon: Lifetime • Cycle: NR • Perspective: Health care system**	<u>Health states/events</u> : • The ADPKD module: - CKD stages 1 to 4 - A significant pain health state - Death • The ESRD module: - CKD stage 5 - Conservative care - HD - PD - Transplant - Death <u>Adverse events</u> : Clinically significant kidney pain	• <b>Tolvaptan:</b> twice daily (up to a maximum total daily dose of 120 mg) The initial daily dose is 60mg tolvaptan as a split-dose regimen (45mg taken upon waking and before breakfast and 15mg taken eight hours later). The initial dose is to be titrated upward to a split-dose regimen of 90mg tolvaptan (60mg+30mg) daily and then to a target split-dose regimen of 120mg tolvaptan (90mg+30mg) daily, if tolerated, with at least weekly intervals between titrations.	TEMPO 3:4 trial	QALY	<u>Type</u> : NR <u>Sources</u> : Literature sources	NR	NR

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				<p>Patients may down-titrate to lower doses based on tolerability. Patients have to be maintained on the highest tolerable tolvaptan dose</p> <ul style="list-style-type: none"> <li>• Placebo</li> </ul>					
<p>Erickson, et al<sup>18</sup> USA</p>	<p>Patients with mild-to-moderate CKD and moderate hypertension but with no other traditional CV risk factors</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> stages 3a-5 according to KDIGO classification</li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> NR</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type:</b> Markov</li> <li>• <b>Time horizon:</b> Lifetime</li> <li>• <b>Cycle:</b> 3 months</li> <li>• <b>Perspective:</b> <ul style="list-style-type: none"> <li>- Base case: NR</li> <li>- PSA: Societal</li> </ul> </li> </ul>	<p><b>Health states/events:</b> Cardiovascular Disease Model:</p> <ul style="list-style-type: none"> <li>• Healthy</li> <li>• CKD stages IIIa-IV</li> <li>• Post MI</li> <li>• Post stroke</li> <li>• Dead</li> <li>• Health events: non-CV death, MI, stroke, remain healthy, die, survive, die from stroke, die from MI</li> </ul> <p>Chronic Kidney Disease Model:</p> <ul style="list-style-type: none"> <li>• Healthy</li> <li>• CKD stages IIIa-IV</li> <li>• Post MI</li> <li>• Post stroke</li> <li>• ESRD</li> <li>• Dead</li> </ul>	<ul style="list-style-type: none"> <li>• Statins</li> <li>• No statins</li> </ul>	<ul style="list-style-type: none"> <li>• Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). 2001</li> <li>• Wolf et al 1991</li> <li>• Burt et al 1995</li> <li>• Go et al 2008</li> <li>• Muntner et al 2002.</li> <li>• USRDS. Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. 2011</li> </ul>	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<p><b>Type:</b> NR</p> <p><b>Sources:</b></p> <ul style="list-style-type: none"> <li>• Gorodetskaya et al 2005</li> <li>• Tengs et al 20000</li> <li>• Assumptions</li> <li>• Fryback et al 1993</li> <li>• Tsevat et al 1993</li> </ul>	<p>3%</p>	<p>3%</p>

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			<ul style="list-style-type: none"> <li>• Health events: die, live, CKD progression, no CKD progression</li> </ul> <p><b>Statin Toxicities Model:</b></p> <ul style="list-style-type: none"> <li>• Statins and No statins</li> <li>• Miopathy</li> <li>• Rhabdomyolysis</li> <li>• Diabetes or memory loss</li> <li>• Dead</li> <li>• Health events: survive, die, develop diabetes or memory loss, myopathy, rhabdomyolysis, survive rhabdomyolysis, die from rhabdomyolysis</li> </ul> <p><u>Adverse events:</u></p> <ul style="list-style-type: none"> <li>• Myalgias</li> <li>• Rhabdomyolysis</li> </ul>						
Adarkwah and Gandjour <sup>67</sup> Germany	<p>Patients with advanced renal insufficiency, proteinuria, and hypertension, but without overt HF</p> <ul style="list-style-type: none"> <li>• eGFR: 15–26 ml/min/1.73 m<sup>2</sup></li> </ul> <p>Based on 2 studies:</p> <ul style="list-style-type: none"> <li>- Hou et al:</li> <li>• ACEi (n = 112): 26.3 ml/min/1.73 m<sup>2</sup></li> <li>• Placebo (n = 112): 25.8 ml/min/1.73 m<sup>2</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: Lifetime (57 years)</li> <li>• Cycle: 1 year, with half-cycle correction applied to both costs and outcomes to</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• Advanced renal disease (serum creatinine: &gt;3.0 mg/dl, GFR: 15–26 ml/min/1.73 m<sup>2</sup>, CKD stage 4)</li> <li>• ESRD</li> <li>• Death</li> </ul> <p><u>Adverse events:</u></p> <ul style="list-style-type: none"> <li>• Base case: Not included</li> <li>• SA: included, but not specified</li> </ul>	<ul style="list-style-type: none"> <li>• ACE inhibitor (patients are treated with benazepril 10 mg twice a day)</li> <li>• Control group (no ACE inhibitor)</li> <li>• Both groups receive other antihypertensive agents (diuretics, a- or b-blockers, calcium-channel</li> </ul>	<ul style="list-style-type: none"> <li>• Advanced renal insufficiency to ESRD with ACE inhibitor:</li> <li>- Hou et al 2006</li> <li>- Ihle et al 1996</li> <li>- Calculations using the Mantel–Haenszel test</li> </ul> <ul style="list-style-type: none"> <li>• Advanced renal insufficiency to ESRD without ACE inhibitor:</li> </ul>	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<p><u>Type:</u> Direct (TTO)</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Hoerger et al 2010</li> <li>• Fryback et al 1993</li> <li>• Churchill et al 1987</li> <li>• Arnesen et al 2004</li> </ul>	3%	3%

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	<p>- Ihle et al:                  • ACEi (n = 36): 14.6 ml/min/1.73 m<sup>2</sup>                  • Placebo (n = 34): 15.8 ml/min/1.73 m<sup>2</sup>                  • Albuminuria:                  Based on 2 studies:                  - Hou et al:                  • ACE inhibitor (n = 112): 1.6                  • Placebo (n = 112): 1.7                  - Ihle et al:                  • ACE inhibitor (n = 36): 2.3                  • Placebo (n = 34): 1.9                  • ACE/ARB: In the ACEi treatment strategy, patients are treated with benazepril 10 mg twice a day</p>	<p>allow for transition events occurring midway through each cycle                  • Perspective: Third-party payer</p>		<p>antagonists, or some combination of these medications), but no other RAAS agents</p>	<p>calculated based on Hou et al and Ihle et al                  • Advanced renal insufficiency to death:                  Statistisches Bundesamt. Sterbetafel 2005/2007 Deutschland                  • ESRD to death: Frei et al 2006</p>				
<p>Clement, et al<sup>68</sup>                  Canada</p>	<p>Anaemic non-dialysis and dialysis patients with CKD                  • eGFR:                  - DD cohort: NR                  - NDD cohort: mean 18.2 (6.6) ml/min/1.73 m<sup>2</sup>                  • <u>Albuminuria</u>: NR                  • <u>ACE/ARB</u>: NR</p>	<p>• Type: Markov                  • Time horizon: Lifetime                  • Cycle: 1 year                  • Perspective: Health care payer</p>	<p><u>Health states/events</u>:                  • Alive, not on dialysis (NDD)                  • Dialysis                  • Continue dialysis                  • Transplanted                  • Dead***  <u>Adverse events</u>:                  Not included/NR</p>	<p>• Use of ESAs to attain a low haemoglobin level target (9-10.9 g/dL)                  • Use of ESAs to attain an intermediate haemoglobin level target (11-12 g/dL)</p>	<p>• CORR: Treatment of End-Stage Organ Failure in Canada 2002 and 2003. Ottawa, Canada: Canadian Institutes of Health Information; 2005.                  • AKDN</p>	<p>QALY</p>	<p><u>Type</u>: Indirect/NR (SF-36, NR)  <u>Sources</u>:                  • Clement et al 2009                  • Manns et al 2003                  • Laupacis Aet al 1996</p>	<p>5%</p>	<p>5%</p>

eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

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				<ul style="list-style-type: none"> <li>• Use of ESA to attain a high haemoglobin level target (&gt;12 g/dL)</li> <li>• Management of anaemia without ESAs (ie., use of rescue blood transfusions as needed)</li> </ul>	<ul style="list-style-type: none"> <li>• Tonelli et al 2006</li> <li>• Wolfe et al 1999</li> </ul>		<ul style="list-style-type: none"> <li>• RCTs (meta-analysis based results):</li> <li>- Drueke et al 2006</li> <li>- Singh et al 2006</li> <li>- Levin et al 2005.</li> <li>- Roger et al 2004.</li> <li>- Rossert et al 2006</li> <li>- Pfeffer et al 2009</li> <li>- Ritz et al 2007</li> <li>• Conversion scale for SF-36: Fryback et al 1997</li> </ul>		
Hayashino, et al <sup>69</sup> Japan	<p>Patients with type 2 diabetes and stages 3 and 4 CKD</p> <ul style="list-style-type: none"> <li>• <u>eGFR</u>: NR</li> <li>• <u>Albuminuria</u>: NR</li> <li>• <u>ACE/ARB</u>: NR</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: Lifetime</li> <li>• Cycle: 1 year</li> <li>• Perspective: Societal</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• CKD</li> <li>• ESRD</li> <li>• Death</li> </ul> <p><u>Adverse events:</u></p> <p>Not included/NR</p>	<ul style="list-style-type: none"> <li>• AST-120 6 g/day + standard care (antihypertension medication alone (either or both ACEi and ARB) + low-protein diet</li> <li>• SOC (antihypertension medication alone (either or</li> </ul>	Akizawa et al 2009	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<p><u>Type:</u></p> <p>NR</p> <p><u>Sources:</u></p> <p>Lawrence et al 1995</p>	3%	3%



eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

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				both ACEi and ARB) + low-protein diet					
Nuijten, et al <sup>70</sup> UK	Hypothetical cohort of patients diagnosed with CKD with SHPT • <u>eGFR</u> : stages 1-5 according to KDIGO classification • <u>Albuminuria</u> : NR • <u>ACE/ARB</u> : NR	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: - Reference case analysis: 10 years</li> <li>- Scenario analysis: lifetime</li> <li>• Cycle: 1 year</li> <li>• Perspective: Health care system</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>•CKD-3-no SHPT and CKD-3-no SHPT-proteinuria</li> <li>• CKD-4-no SHPT and CKD-4-no SHPT-proteinuria CKD-3-SHPT</li> <li>• CKD-3-SHPT-proteinuria</li> <li>• CKD-4-SHPT and CKD-4-SHPT-proteinuria</li> <li>• No CKD</li> <li>• CKD-1-diagnosed and CKD-1-undiagnosed</li> <li>• CKD-2-diagnosed and CKD-2-undiagnosed</li> <li>• CKD-3-undiagnosed</li> <li>• CKD-4-undiagnosed</li> <li>• CKD 5</li> <li>• CKD dialysis</li> <li>• CKD-transplantation.</li> <li>• Dead</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• Paricalcitol</li> <li>• Alfacalcidol</li> </ul>	Keith et al 2002	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<p><u>Type:</u> Direct (TTO)</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Gorodetskaya et al 2005</li> <li>• Roderick et al 2005</li> <li>• Hogan et al 2002</li> </ul>	3.5%	3.5%
Nuijten, et al <sup>71</sup> USA	Virtual cohort of CKD patients with SHPT and proteinuria	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon:</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>•CKD 1</li> <li>• CKD 2</li> <li>• CKD 3</li> </ul>	<ul style="list-style-type: none"> <li>• Paricalcitol</li> <li>• Calcitriol</li> <li>• Cinacalcet</li> </ul>	<ul style="list-style-type: none"> <li>• Keith et al 2002</li> <li>• Calculated based on Teng et al 2003</li> <li>• Bakris et al 2005</li> </ul>	<ul style="list-style-type: none"> <li>• LYG</li> <li>• QALY</li> </ul>	<p><u>Type:</u> NR</p> <p><u>Sources:</u></p>	3.5%	3.5%

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	<ul style="list-style-type: none"> <li>• <b>eGFR:</b> <ul style="list-style-type: none"> <li>- Stage 2: GFR <math>\geq</math>60 ml/min/1.73 m<sup>2</sup></li> <li>- Stage 3: 30 <math>\leq</math>GFR &lt;60 ml/min/1.73 m<sup>2</sup></li> <li>- Stage 4: 15 <math>\leq</math>GFR &lt;30 ml/min/1.73 m<sup>2</sup>"</li> </ul> </li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> The model is based on data by Golan, which allows the incorporation of preventive treatment (ACEi/ARB); costs of both ACEi and ABR included in the analysis</li> </ul>	<ul style="list-style-type: none"> <li>- Base case: 10 years</li> <li>- Scenario analyses: lifetime</li> <li>• Cycle: 1 year</li> <li>• Perspective: <ul style="list-style-type: none"> <li>- Base case: third-party payer</li> <li>- Scenario analysis: societal</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• CKD 4</li> <li>• CKD 5 dialysis</li> <li>• CKD 5 transplantation</li> <li>• Dead</li> <li>• Hospitalization (health event)</li> </ul> <p>Health states are further subdivided by undiagnosed and diagnosed of CKD; undiagnosed and diagnosed SHPT; proteinuria (macro and microalbuminuria); diabetes, hypertension, diabetes and hypertension, or neither; use of ACEi, ARB, and/or VDRA therapy; and HD or PD with in CKD5 dialysis stage.</p> <p><u>Adverse events:</u> Not included/NR</p>		<ul style="list-style-type: none"> <li>• Smith et al 2004</li> <li>• Kalantar-Zadeh et al 2006</li> </ul>		<ul style="list-style-type: none"> <li>• Gorodetskaya et al 2005</li> <li>• Hogan et al 2002</li> </ul>		
Hogan, et al 72 USA	<p>Patients with renal impairment and hypertension</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> <ul style="list-style-type: none"> <li>- Mild renal insufficiency (creatinine clearance 45-60 ml/min) [n = 227]</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: 7 years</li> <li>• Cycle: 1 year</li> <li>• Perspective:</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• Chronic renal impairment</li> <li>• Dialysis</li> <li>• Renal transplantation</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• Routine antihypertensive therapy + benazepril</li> <li>• Routine antihypertensive therapy + placebo</li> </ul>	AIPRI study	QALY	<p><u>Type:</u> NR</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Hathaway et al 1998</li> <li>• Gorlen et al 1993</li> <li>• Simmons et al 1988</li> </ul>	3%	3%

eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

From a supplement to *The American Journal of Managed Care*<sup>®</sup>: “Patients With Diabetes and Chronic Kidney Disease: ACE Inhibitor or ARB Treatment, Medical Costs for Disease Management, and the FINE-CKD Model to Evaluate Economic Value of Finerenone”

	<p>- Moderate (creatinine clearance 30-45 ml/min) [n = 356]</p> <ul style="list-style-type: none"> <li>• <b>Albuminuria:</b> Urinary protein excretion (g/day):</li> <li>- Benazepril: 1.8 (2.6)</li> <li>- Placebo: 1.8 (2.2)</li> <li>• <b>ACE/ARB:</b> ACEi (Benazepril)</li> </ul>	Health care payer					<ul style="list-style-type: none"> <li>• Morris et al 1988</li> <li>• Churchill et al 1987</li> <li>• Laupacis et al 1996</li> </ul>		
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**eAppendix Table 5.** Overview of cost-effectiveness models studying screening for CKD

Author, year, country	Study population (eg, eGFR, albuminuria, ACE/ARB)	Model summary (type, time horizon, cycle length, perspective)	Health states /events and adverse events list	Treatment arms	Transition probability sources	Efficacy measure	Utility types and source	Discount rate for cost	Discount rate for effect
Go, et al <sup>16</sup> Korea	<p>Patients with progressing CKD</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> NR</li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> ACEi</li> </ul> <p>were inputted as treatment for CKD G4/G5:</p> <ul style="list-style-type: none"> <li>- Treatment effects on CKD progression reduction: 0.67 [0.54–0.84]</li> <li>- Treatment effects on CVD events reduction: 0.81 [0.73–0.89]</li> <li>- Treatment effects on mortality reduction: 0.93 [0.73–1.10]</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type:</b> Markov</li> <li>• <b>Time horizon:</b> Lifetime</li> <li>• <b>Cycle length:</b> 1 year</li> <li>• <b>Perspective:</b> Societal</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• State 0: CKD G2 or less</li> <li>• CKD G3</li> <li>• CKD G4</li> <li>• CKD G5</li> <li>• HD</li> <li>• PD</li> <li>• KT 1st year</li> <li>• Post KT</li> <li>• MI 1st year</li> <li>• Post MI, stroke 1st year</li> <li>• Post stroke</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• Current screening (dipstick + eGFR, screening interval 2 years, starting age 40 years)</li> <li>• No screening</li> </ul>	<ul style="list-style-type: none"> <li>• Tsai 2016</li> <li>• Jafar 2003</li> <li>• Jin 2015</li> <li>• Kim, 2013</li> <li>• Woodward 2003</li> <li>• Singh, 2013</li> <li>• Go, 2004</li> <li>• Kim 2015</li> <li>• Chen 2014</li> <li>• Statistics Korea, 2013</li> <li>• Jeon, 2015</li> <li>• NHIS-cohort</li> </ul>	QALY	<p><u>Utility type:</u> Direct (SG)</p> <p><u>Sources:</u> Survey of 300 Koreans in February 2016</p>	5%	5%
Ravaghi, et al <sup>73</sup> Iran	<p>Iranian adult population</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> NR</li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> NR</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type:</b> Markov</li> <li>• <b>Time horizon:</b> NR</li> <li>• <b>Cycle length:</b> NR</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• Stage 1</li> <li>• Stage 2</li> <li>• Stage 3</li> <li>• Stage 4</li> </ul>	<ul style="list-style-type: none"> <li>• Screening for CKD: The screening process is based on the GFR, whose initial calculation is by</li> </ul>	<ul style="list-style-type: none"> <li>• Black et al 2010</li> <li>• Patients’ electronic records file and after the</li> </ul>	QALY	<p><u>Utility type:</u> NR</p> <p><u>Sources:</u> Black et al 2010</p>	5%	5%

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		<ul style="list-style-type: none"> <li>• Perspective: Third-party payer</li> </ul>	<ul style="list-style-type: none"> <li>• Stage 5</li> <li><u>Adverse events:</u> Not included/NR</li> </ul>	<ul style="list-style-type: none"> <li>measuring blood creatinine, followed by an analysis of urine creatinine and volume. If the results confirm CKD, the kidney ultrasound is requested</li> <li>• Nonscreening for CKD</li> </ul>	<ul style="list-style-type: none"> <li>panel between nephrologists and health economics experts</li> <li>• Prevalence data in Iran</li> </ul>				
<p>Critselis, et al<sup>74</sup></p> <p>Europe</p>	<p>Diabetic patients with low or high risk of CKD progression (micro- or macroalbuminuria and/or diabetic nephropathy) or any of the health outcomes (ESKD, dialysis, renal transplantation or death)</p> <ul style="list-style-type: none"> <li>• <u>eGFR</u>: NR</li> <li>• <u>Albuminuria</u>: Mixed</li> <li>• <u>ACE/ARB</u>: NR</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: Lifetime (40 years)</li> <li>• Cycle length: NR</li> <li>• Perspective: Health care system</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• T2DM (without CKD)</li> <li>• Annual screening for CKD progression</li> <li>• CKD progression (Microalbuminuria)</li> <li>• CKD progression (Macroalbuminuria/ diabetic nephropathy)</li> <li>• Intensified therapy</li> <li>• Event-free survival</li> <li>• ESKD</li> <li>• Dialysis</li> </ul>	<ul style="list-style-type: none"> <li>• Annual screening strategy based on the CKD273 classifier: applied at baseline and annually thereafter in all patients until either CKD progression (micro- or macroalbuminuria and/or diabetic nephropathy) or any of the health outcomes (ESKD, dialysis, renal transplantation or death) under evaluation occurred.</li> <li>• Annual UAE-based screening: applied at baseline</li> </ul>	<ul style="list-style-type: none"> <li>• UKPDS 64</li> <li>• Kainz et al 2015</li> <li>• Manns et al 2010</li> </ul>	QALY	<p><u>Utility type:</u> NR</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Kennedy-Martin et al 2015</li> <li>• Lung et al 2011</li> </ul>	NR	NR

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			<ul style="list-style-type: none"> <li>• Renal transplantation</li> <li>• Death due to any cause or CVD</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	and annually thereafter in all patients until either CKD progression (micro- or macroalbuminuria and/or diabetic nephropathy) or any of the health outcomes (ESKD, dialysis, renal transplantation or death) under evaluation occurred.					
Ferguson, et al <sup>75</sup> Canada	<p>Rural Canadian indigenous adults</p> <ul style="list-style-type: none"> <li>• <u>eGFR</u>: according to KDIGO classification</li> <li>• <u>Albuminuria</u>: UACR (mg/mmol): <ul style="list-style-type: none"> <li>- All communities: 1.4 (0.6–3.2)</li> <li>- Road access: 1.0 (0.5–1.9)</li> <li>- Air access only: 1.9 (0.8–5.1)</li> </ul> </li> <li>• <u>ACE/ARB</u>: ACEis and ARBs were assumed to offer benefit only in individuals with severely increased albuminuria. They</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: Lifetime (45 years)</li> <li>• Cycle length: 1 year</li> <li>• Perspective: Health care payer</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• Normal kidney function</li> <li>• Low risk of progression to kidney failure</li> <li>• Intermediate risk of progression to kidney failure</li> <li>• High risk of progression to kidney failure</li> <li>• Dialysis</li> <li>• transplant</li> <li>• Death</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• One-off screening (eGFR and UACR) and risk-based treatment for CKD</li> <li>• SOC</li> </ul>	<ul style="list-style-type: none"> <li>• KDIGO 2012</li> <li>• Hemmelgarn et al 2009</li> <li>• CORR report 2014.</li> </ul>	QALY	<p><u>Utility type:</u> NR</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Manns et al 2010</li> <li>• Laupacis et al 1996</li> <li>• Gorodetskaya et al 2005</li> </ul>	5%	5%

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	assumed treatment offers a 23% relative risk reduction to mortality rates and 33% relative risk reduction in rates of progression to kidney failure and assumed equivalent outcomes for both ACE-Is and ARBs								
Hoerger, et al 76 USA	<p>Patients (African Americans and non-African Americans) at risk for CKD</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> Stages according to KDIGO classification; normal: &gt;60 ml/min/1.73 m<sup>2</sup></li> <li>• <b>Albuminuria:</b> The model tracks kidney damage based on persistent microalbuminuria (sustained ACR between 30 and 299 mg/g) and macroalbuminuria (ACR ≥300 mg/g)</li> <li>• <b>ACE/ARB:</b> The effect of ACE/ARB therapy on persons with microalbuminuria is assumed to be a 55%</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type:</b> discrete state simulation</li> <li>• <b>Time horizon:</b> Lifetime (60 years)</li> <li>• <b>Cycle length:</b> NR</li> <li>• <b>Perspective:</b> NR</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• No CKD</li> <li>• CKD stage1</li> <li>• CKD stage2</li> <li>• CKD stage3</li> <li>• CKD stage4</li> <li>• C2D stage 5</li> <li>• Death</li> <li>• Discrete medical events that are tracked include stroke and coronary heart disease, including MI and angina</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• Screening for microalbuminuria</li> <li>• SOC</li> </ul>	<ul style="list-style-type: none"> <li>• NHANES data from 1999–2006</li> <li>• Adler et al 2003</li> <li>• Sacco et al 1994</li> <li>• Strippoli et al 2004</li> <li>• Hoerger et al 2010</li> <li>• Hoerger et al 2010</li> </ul>	QALY	<p><u>Utility type:</u> Direct (TTO)</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Boulware et al 2003</li> <li>• Gorodetskaya et al 2005</li> </ul>	3%	3%

eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

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	<p><b>reduction in the probability of progression from micro- to macroalbuminuria</b>  <b>Each person who undergoes screening receives an initial quantitative microalbuminuria screening test. If the first test returns positive, a second confirmatory test is administered as well as tests to estimate GFR. Once microalbuminuria has been confirmed, persons with GFR less than 60 receive additional tests to determine the cause of CKD and then receive ACE or ARB therapy. On the other hand, persons with GFR greater than or equal to 60 proceed directly from the confirmation of microalbuminuria to ACE or ARB therapy</b></p>								
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<p>Howard, et al 77 Australia</p>	<p>Persons at increased risk of progressive kidney disease</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> NR</li> <li>• <b>Albuminuria:</b> <ul style="list-style-type: none"> <li>- No Albuminuria</li> <li>- Microalbuminuria</li> <li>- Macroalbuminuria</li> </ul> </li> <li>• <b>ACE/ARB:</b> <ul style="list-style-type: none"> <li>- ACEi was added in known diabetics as improved management</li> <li>- Screen-detected proteinuria persons were treated with ACEi</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Type:</b> Markov</li> <li>• <b>Time horizon:</b> Lifetime (up to 95 years of age)</li> <li>• <b>Cycle length:</b> 1 year</li> <li>• <b>Perspective:</b> Health care payer</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• <b>Improved management strategies:</b> <ul style="list-style-type: none"> <li>- Hypertension (with or without proteinuria)</li> <li>- CKD</li> <li>- ESKD requiring RRT</li> <li>- Dialysis</li> <li>- Transplant</li> <li>- Death</li> </ul> </li> <li>• <b>Screening + improved management strategies:</b> <ul style="list-style-type: none"> <li>- Diabetes no albuminuria (with or without hypertension)</li> <li>- Diabetes microalbuminuria (with or without hypertension)</li> <li>- Diabetes macroalbuminuria (with or without hypertension)</li> <li>- CKD</li> <li>- ESKD requiring RRT</li> <li>- Dialysis</li> <li>- Transplant</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Improved management in known/existing patients:</b> <ul style="list-style-type: none"> <li>- Intensive glycemic control in known diabetic patients</li> <li>- Addition of an ACE inhibitor in known diabetics</li> <li>- Intensive blood pressure control in known hypertensive patients</li> </ul> </li> <li>• <b>Primary care–based screening for CKD risk factors:</b> <ul style="list-style-type: none"> <li>- Screening (50–69 years) for diabetes and intensive glycaemic control in known and screen-detected diabetic patients</li> <li>- Screening (50–69 years) for hypertension and intensive blood pressure control in known and screen-detected hypertensive patients</li> </ul> </li> </ul>	<p>AusDiab:</p> <ul style="list-style-type: none"> <li>• Briganti et al 2003 135–9.</li> <li>• Colagiuri et al 2004</li> </ul>	<p>QALY</p>	<p><u>Utility type:</u> Indirect (SF-6D)</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Howard et al</li> <li>• Lee et al 2005</li> <li>• Laupacis et al 1996</li> <li>• Cost-Effectiveness Analysis (CEA) Registry (Centre for the Evaluation of Value and Risk in Health)</li> </ul>	<p>5%</p>	<p>5%</p>
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			- Death <u>Adverse events:</u> Not included/NR	- Screening (50–69 years) for proteinuria and addition of an ACE inhibitor in all known diabetics and screen-detected • Corresponding SOC					
Manns, et al 78 Canada	<p>Adults with no previous assessment of GFR</p> <p>• <u>eGFR</u>:*</p> <p>Percentages of patients in stages:</p> <ul style="list-style-type: none"> <li>• None (<math>\geq 60</math> ml/min/1.73 m<sup>2</sup>)</li> <li>- Overall: 235 160 (81%)</li> <li>- With diabetes: 19 788 (65%)</li> <li>- Without diabetes: 215 372 (83%)</li> <li>• Stage 3 (30-59.9 ml/min/1.73 m<sup>2</sup>)</li> <li>- Overall: 51 591 (18%)</li> <li>- With diabetes: 9162 (30%)</li> <li>- Without diabetes: 42 429 (16%)</li> <li>• Stage 4 (15-29.9 ml/min/1.73 m<sup>2</sup>)</li> <li>- Overall: 2962 (1%)</li> </ul>	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: Lifetime</li> <li>• Cycle length: 1 year</li> <li>• Perspective: Health care system</li> </ul>	<p><u>Health states/events:</u></p> <ul style="list-style-type: none"> <li>• People without CKD</li> <li>• People non-dialysis CKD</li> <li>• Patients receiving dialysis</li> <li>• Patients with a functioning transplant</li> </ul> <p><u>Adverse events:</u> Not included/NR</p>	<ul style="list-style-type: none"> <li>• One-off population-based screening for CKD</li> <li>• No screening</li> </ul>	<ul style="list-style-type: none"> <li>• Garg et al 2002</li> <li>• Hemmelgarn et al 2009.</li> <li>• National Center for Health Statistics. Plan and operation of the Third National Health and Nutrition Examination Survey, 1988-94. Vital Health Stat 1994;1:1-407.</li> <li>• Manns et al 2001</li> <li>• Levey et al 1999</li> </ul>	<ul style="list-style-type: none"> <li>• QALY</li> <li>• Cases of ESRD prevented</li> </ul>	<p><u>Utility type:</u> NR</p> <p><u>Sources:</u></p> <ul style="list-style-type: none"> <li>• Gorodetskaya et al 2005</li> <li>• Laupacis et al 1996</li> <li>• Manns et al 2003</li> <li>• Manns et al 2005</li> </ul>	5%	5%

eAppendix: FINE-CKD Model to Evaluate Economic Value of Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes

From a supplement to *The American Journal of Managed Care*<sup>®</sup>: “Patients With Diabetes and Chronic Kidney Disease: ACE Inhibitor or ARB Treatment, Medical Costs for Disease Management, and the FINE-CKD Model to Evaluate Economic Value of Finerenone”

	<ul style="list-style-type: none"> <li>- With diabetes: 1000 (3%)</li> <li>- Without diabetes: 1962 (1%)</li> <li>• Stage 5 (&lt;15 ml/min/1.73 m<sup>2</sup>)</li> <li>- Overall: 900 (0%)</li> <li>- With diabetes: 327 (1%)</li> <li>- Without diabetes: 573 (0%)</li> <li>• <u>Albuminuria</u>: NR</li> <li>• <u>ACE/ARB</u>: The authors assumed that people found to have chronic kidney disease would receive an ACEi or angiotensin blocker (if tolerated), with a target blood pressure of &lt;130/ 80 mm Hg. The authors assumed that 75% of people are treated with ACEi (generic ramipril \$0.63/day), and 25% with angiotensin blockers (irbesartan \$1.21/ day)</li> </ul>				<ul style="list-style-type: none"> <li>• Hux et al 2002</li> <li>• Quan et al 2002</li> <li>• Quan et al 2005</li> </ul>				
Boulware, et al <sup>79</sup> USA	US adults aged 50 years presenting to a primary care physician for an annual physical examination with	<ul style="list-style-type: none"> <li>• Type: Markov</li> <li>• Time horizon: NR</li> <li>• Cycle length: NR</li> </ul>	<u>Health states/events</u> : <ul style="list-style-type: none"> <li>• Normal kidney function</li> <li>• CKD stage 1</li> </ul>	• Strategy of annual screening for proteinuria and subsequent treatment with		QALY	<u>Utility type</u> : Direct (SG or TTO)  <u>Sources</u> :	3%	3%

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	<p>previously undetected proteinuria</p> <ul style="list-style-type: none"> <li>• <b>eGFR:</b> According to KDIGO classification</li> <li>• <b>Albuminuria:</b> NR</li> <li>• <b>ACE/ARB:</b> Positive quantitative urine protein test results would prompt either subsequent treatment by a primary care physician with an ACE inhibitor or ARB therapy for persons with nor-mal renal function or referral to and evaluation by a nephrologist followed up by treatment with an ACEi or ARB therapy for persons with depressed renal function</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Perspective:</b> Societal</li> </ul>	<ul style="list-style-type: none"> <li>• CKD stage 2-4</li> <li>• ESRD</li> <li>• Death</li> </ul> <p><u>Adverse events:</u></p> <ul style="list-style-type: none"> <li>• Anaphylaxis secondary to ACEi or ARB</li> <li>• Angioedema secondary to ACEi</li> </ul>	<p>ACEi or ARB therapy</p> <ul style="list-style-type: none"> <li>• Strategy of routine clinical practice (no screening)</li> </ul>			<ul style="list-style-type: none"> <li>• <b>Assumption</b></li> <li>• Tengs et al 2000</li> <li>• de Wit et al 2002"</li> </ul>		
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