

An epidemiological and economic simulation model to evaluate strategies for the control of bovine virus diarrhea in Germany

Supplementary material

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Table S1: Input parameters and distributions used in the Gross margin analysis (GMA).

Parameter	Unit	Notation	Calculation/ value/ distribution	References/ comments
Gross Margin for a dairy farm	Euro	GM	$GM = R - VC$	
Revenues	Euro	R	$R = R_{milk} + R_{ani} + R_{man}$	
Revenues for selling milk	Euro	R_{milk}	$R_{milk} = my * ms * mp$	
annual milk yield healthy animal	kg/cow	my	$my = rnorm(10000, 7087.25, 136.11)$	Normal distribution based on data from Federal statistical office (Destatis) on milk yield on district level 2011-2015
influence BVD infection on milk yield	kg/cow	imy	$imy = my * rlnorm(10000, log(0.01), 0.008)$	The decrease in milk yield was estimated at about 70 liters.
annual milk yield BVDV infected animal	kg/cow	my_{BVD}	$my_{BVD} = my * \frac{(Ci - 60)}{(Ci_{BVD} - 60)} - imy$	The annual milk yield for an infected animal includes the reduction of the milk yield due to acute symptoms as well as the reduction caused by a prolonged calving interval
proportion of milk sold	%		$ms = 95$	Destatis: milk sold on district level 2011-2015
Milk price	Euro/kg	Mp	$mp = dUnif(0.289082, 0.360424)$	Uniform distribution based on data from Federal Ministry of Food and Agriculture; BLE: monthly average milk prices on federal state level
Revenues for selling animals	Euro	R_{ani}	$R_{ani} = R_{calf} + R_{cow}$	
Revenues from calf sale	Euro	R_{calf}	$R_{calf} = CC * p_{mc} * r + CC * p_{fc} * (1 - r)$	
number of calves per cow	n	CC	$CC = \frac{365}{Ci} - \frac{365}{Ci * cm_y}$	
price male calf	Euro	p_{mc}	$p_{mc} = dTri(80.94, 121.41, 105.22)$	Betriebsplanung Landwirtschaft 2014/15, KTBL: price for 14 days old calves
price female calf	Euro	p_{fc}	$p_{fc} = dTri(30.35, 60.70, 44.52)$	
male/female ratio	ratio	R	$r = 0.5$	Estimated
Revenues from cow sale	Euro	R_{cow}	$R_{cow} = (pC * wC - mC) * (1 - CM) * RR$	
price slaughter cow	Euro/kg	pC	$pC = 2.05$	Bavarian State Research Centre for Agriculture, Bayerische Landesanstalt für Landwirtschaft https://www.stmelf.bayern.de/idb/vergleiche.html
average weight of a slaughter cow	kg	wC	$wC = 326.46$	
marketing costs of a cow	Euro	mC	$mC = 21$	
cow mortality	ratio	CM	$CM = 0.054$	
replacement rate	ratio	RR	$RR = 0.33$	Bayerische Landesanstalt für Landwirtschaft, https://www.stmelf.bayern.de/idb/vergleiche.html

calving interval healthy animal	days	Ci	$Ci = dTri(376, 417, 458)$	Triangle distribution based on data from HI Tier
calving interval with BVD infection	days	Ci_{BVD}	$Ci_{BVD} = Ci + iCi_{BVD}$	
calf mortality	ratio	cm	cm = 0.1	fixed based on data from Bayerische Landesanstalt für Landwirtschaft, https://www.stmelf.bayern.de/idb/vergleiche.html
influence of BVD infection on calf mortality	ratio	icm	icm = 0.1	
calf mortality with BVD infection	ratio	cm_{BVD}	$cm_{BVD} = cm + icm$	
increased calving interval (additional number of days) in case of transient BVD infection	days	iCi_{BVD}	$iCi_{BVD} = lnorm(log(10.5), log(2))$	iCi_{BVD} is assumed as log normal distribution to increase about 13 days on average. Estimated based on (Burgstaller et al., 2016; Viet et al., 2004).
Revenues for selling manure	Euro	R_{man}	$R_{man} = 111.1$	Fixed (based on data of the Bavarian State Research Centre for Agriculture, Bayerische Landesanstalt für Landwirtschaft; https://www.stmelf.bayern.de/idb/vergleiche.html)
Variable Costs	Euro	VC	$VC = VCR_y + VCfe_y + VCcr_y + VCvet_y + VCbio_y + VCins_y + VCmach_y + VCmisc_y$	
Variable Costs for restocking per year	Euro	VCR_y	$VCR_y = (p_h + m_h) * RR$	
price for a heifer	Euro	p_h	$p_h = 1,950$	Fixed (based on data of the Bavarian State Research Centre for Agriculture, Bayerische Landesanstalt für Landwirtschaft; https://www.stmelf.bayern.de/idb/vergleiche.html)
marketing costs for a heifer	Euro	m_h	$m_h = 33$	
Variable Costs for feed per year	Euro	$VCfe_y$	$VCfe_y = \frac{my - my_f}{ef_{con} * p_{con}}$	
milk yield from forage	kg	my_f	$my_f = \frac{(f_u * f_q - bmr)}{mf}$	
Forage uptake per year	kg	f_u	$f_u = 4562.5$	Fixed (based on data of the Bavarian State Research Centre for Agriculture, Bayerische Landesanstalt für Landwirtschaft; https://www.stmelf.bayern.de/idb/vergleiche.html)
Forage quality	factor	f_q	$f_q = 5.9$	
milk per kg forage	factor	mf	$mf = 3.3$	
basal metabolic rate	MJ	bmr	$bmr = 15300$	
efficiency of concentrate use	l/kg	ef_{con}	$ef_{con} = rtri(niteration, 1.7, 2, 1.9)$	

price for feed concentrates	Euro/kg	p_{con}	$p_{con} = 0.28$	Fixed (based on data of the Bavarian State Research Centre for Agriculture, Bayerische Landesanstalt für Landwirtschaft)
Variable Costs for calf rearing per year	Euro	$VCcr_y$	$VCcr_y = 57.66$	Fixed (based on data of the Bavarian State Research Centre for Agriculture, Bayerische Landesanstalt für Landwirtschaft; https://www.stmelf.bayern.de/idb/vergleiche.html)
Variable Costs for veterinary treatment per year	Euro	$VCvet_y$	$VCvet_y = 165$	
Variable Costs for water and electricity per year	Euro	$VCwa_y$	$VCwa_y = 75.63$	
Variable Costs for artificial insemination per year	Euro	$VCins_y$	$VCins_y = 9.41$	
Variable Costs for machines per year	Euro	$VCmach_y$	$VCmach_y = 58.82$	
Variable Costs, miscellaneous (dues) per year	Euro	$VCmisc_y$	$VCmisc_y = 36.13$	
Direct Costs per TI animal	Euro	DC_{TI}	$DC_{TI} = GM_h - GM_{TI}$	The GM for a healthy animal (GM_h) and TI animal (GM_{TI}) are calculated using equation 1

Table S2: Input parameters used in the animal valuation model to estimate the market value of PI animals (cows, young stock, calves).

Parameter	Unit	Notation	Calculation/ value/ distribution	References/ comments
market value of a cow	Euro	vc_y	$vc_y = B \times (1 + bp + mp + ib + da + p + c) + m$	based on the data provided by the chamber of agriculture of North-Rhine-Westphalia
Basic value	Euro	B		
depreciation for not being registered in a breeding program	per cent	bp	$bp = -10$	
depreciation for not being included in a milk inspection program	per cent	mp	$mp = -30$	According to http://milchwirtschaft.de/ , in 2014 88% of all German dairy cows were included in the milk inspection program (Milchleistungsprüfung)
depreciation for not being free of infectious bovine rhinotracheitis	per cent	ib	$ib = -10$	
depreciation according to the age of the animal	per cent	da	$da = -10 - -40$	We used 1-month age groups. According to HIT, the age distribution was as follows: 65 % of the animals were 3-6 years; 15 % 6-7 years; 7% 7-8 years; 5% 8-9 years; 0.07 >9 years.
premium for pregnancy status	per cent	p	$p = \begin{cases} 0, & < 4 \text{ months} \\ 4, & \geq 4 \text{ months} \\ 8, & \geq 6 \text{ months} \end{cases}$	we assumed that a cow will gain a bonus of 0.04 for 4 month per year (4-7 months pregnant) and 0.08 for two month per year (8-9 months pregnant).
premium for general body condition	per cent	c	$c = 4$	For each point above a body condition of 80
premium for milk protein	Euro	m	$m = \begin{cases} 0, & = \text{average} \\ 4 \text{ per kg}, & > \text{average} \\ -4 \text{ per kg}, & < \text{average} \end{cases}$	4 € for each kg above-average, -4 € for each kg below-average
market value of a calf or young stock per year	Euro	vy_y	$vy_y = 0.2 * (B * (1 + c) + m) + \frac{(B * (1 + c) + m) - 0,2 * (B * (1 + c) + m)}{afc} \times a$	
age at first calving of the mother	months	afc	$afc = 28$	fixed value
age of the animal	months	a		

Table S3: Input parameters and equations used in the economic model.

Parameter	Notation	Calculation/ value/ distribution	References/ comments
Total Costs of BVD for the 20-year period 2011-2030 in each scenario	CT_s	$CT_s = \sum_{y=2011}^{2030} DC_{y,s} + IC_{y,s}$	
Total Costs of BVD per year in each scenario	$CT_{y,s}$	$CT_{y,s} = DC_{y,s} + IC_{y,s}$	
Direct Costs of BVD per year in each scenario	$DC_{y,s}$	$DC_{y,s} = DCPI_{y,s} + DCTI_{y,s}$	
Direct Costs incurred by PIs per year in each scenario	$DCPI_{y,s}$	$DCPI_{y,s} = DCPIc_{y,s} + DCPIy_{y,s} + DCPIh_{y,s} + DCPIc_{y,s}$	Includes the market value of animals that die due to a persistent BVDV infection (e.g. due to Mucosal disease), disposal costs of these dead animals, and veterinary costs.
Direct Costs PI calves	$DCPIc_{y,s}$	$DCPIc_{y,s} = n_{PIc_{y,s}} * C_{PI}$	
Direct Costs PI young cattle	$DCPIy_{y,s}$	$DCPIy_{y,s} = n_{PIy_{y,s}} * C_{PI}$	
Direct Costs PI heifers	$DCPIh_{y,s}$	$DCPIh_{y,s} = n_{PIh_{y,s}} * C_{PI}$	
Direct Costs PI cows	$DCPIC_{y,s}$	$DCPIC_{y,s} = n_{PIC_{y,s}} * C_{PI}$	At the level of the national livestock sector, studies indicated a loss due to BVDV under endemic conditions of € 15-20 per cow present (Anonymus, 2001)
number of PI calves, young stock, heifers, and cows respectively per year in each scenario	$n_{PIc_{y,s}}$ $n_{PIy_{y,s}}$ $n_{PIh_{y,s}}$ $n_{PIC_{y,s}}$		Calculated in the DSM (using 1-month age groups). According to the age, animals were categorized as calves (0-6 months), young cattle (7-18 months), heifers (19-28 months), and cows (older than 29 months).
average direct costs per PI animal	C_{PI}	$C_{PI} = vet_{PI} + pd_{PI}$	
costs of veterinary treatment of a PI animal	vet_{PI}	Triangle distribution (27.50; 36.10; 72.70)	Include travel costs, clinical examination and advice, one injection/ infusion, and antibiotic treatment. As per current legal framework (German veterinary fee schedule, <i>Gebührenordnung für Tierärzte</i>), veterinarians may charge travel costs of 2.30 € per double km (minimum of 8,60 €). Examination and advice amount to 11.46 to 34.38 €, injection/ infusion to 3.44 to 10.32, and antibiotic treatment to 4-5 €.

costs and lost value through premature death of a PI animal	pd_{PI}	$pd_{PI} = v_c + d_c$	
market value of a dead animal	v_c		Calculated in the animal valuation model
disposal costs (calf, young stock, cow)	d_c, d_y, d_c	calf 7.80 €; young stock, heifer 35.10 €; cow 68.90 €	Fixed values
Direct Costs incurred by TIs per year in each scenario	$DCTI_{y,s}$	$DCTI_{y,s} = DCTIc_{y,s} + DCTIy_{y,s} + DCTIh_{y,s} + DCTIC_{y,s}$	Include production losses
Direct Costs TI calves	$DCTIc_{y,s}$	$DCTIc_{y,s} = n_{TIc_{y,s}} * DCTIa_c$	
Direct Costs TI young cattle	$DCTIy_{y,s}$	$DCTIy_{y,s} = n_{TIy_{y,s}} * DCTIa_y$	
Direct Costs TI heifers	$DCTIh_{y,s}$	$DCTIh_{y,s} = n_{TIh_{y,s}} * DCTIa_h$	
Direct Costs TI cows	$DCTIC_{y,s}$	$DCTIC_{y,s} = n_{TIC_{y,s}} * DCTIa_c$	
number of TI calves, young cattle, heifers, and cows respectively per year in each scenario	$n_{TIc_{y,s}}$ $n_{TIy_{y,s}}$ $n_{TIh_{y,s}}$ $n_{TIC_{y,s}}$		Calculated in the DSM (using 1-month age groups). According to the age, animals were categorized as calves (0-6 months), young cattle (7-18 months), heifers (19-28 months), and cows (older than 29 months).
Direct Costs TI: average production losses incurred per calf	$DCTIa_c$	Uniform distribution (0;10)	
Direct Costs TI: average production losses incurred per young cattle	$DCTIa_y$	Uniform distribution (0;10)	
Direct Costs TI: average production losses incurred per heifer	$DCTIa_h$	Resampling from GMA results	Calculated in the GMA for a heifer (Resampling done randomly with replacement).
Direct Costs TI: average production losses incurred per cow	$DCTIa_c$	Resampling from GMA results	Calculated in the GMA for a cow (Resampling done randomly with replacement).
Indirect Costs of BVD per year in each scenario	$IC_{y,s}$	$IC_{y,s} = ICdi_{y,s} + ICva_{y,s} + ICps_{y,s} + Ictr_{y,s}$	
Indirect Costs incurred by diagnostic measures per year in each scenario	$ICdi_{y,s}$	$ICdi_{y,s} = ICdidt_{y,s} + ICdidb_{y,s} + ICindb_{y,s}$	
Indirect Costs incurred by antigen analysis (direct detection) by tissue sampling (ear tag) per year in each scenario	$ICdidt_{y,s}$	$ICdidt_{y,s} = (n_{t1_{y,s}} * C_{t1}) + (n_{t2_{y,s}} * C_{t2})$	

number of animals tested (ear tag, first (1) application)	$n_{t1y,s}$		calculated in the DSM
Costs antigen detection ear tags, first (1) analysis	C_{t1}	$C_{t1} = c_{t1} + c_p/5 + c_{sh} + c_{ELI1} + c_c$	
costs diagnostic ear tags, first (1) application	C_{t1}	Triangle distribution (3;4;5)	According to Landeskontrollverband Baden-Württemberg: 1,12 € for two ear tags; 0.51 € shipping; 3.60 € laboratory testing; 1.80 € diagnostic material (Anonymus, 2010)
cost ear tag pliers	C_p	Triangle distribution (15; 20; 25) / 5	Costs for ear tag pliers according to Sächsischer Landeskontrollverband; We accounted for one fifth of the costs, since pliers can be used for several animals.
costs shipping	C_{sh}	Triangle distribution (0.1; 0.2; 0.5)	
costs laboratory analysis (ELISA), first (1) test	C_{ELI1}	Triangle distribution (3.5; 4.5; 5.5)	
costs communication of the test result	C_c	Triangle distribution (0.2; 0.4; 0.8)	
number of animals tested (ear tag, second (2) application)	$n_{t2y,s}$		
Costs antigen detection ear tags, second (2) analysis	C_{t2}	$C_{t2} = c_{t2} + c_{ELI2}$	
costs diagnostic ear tags, second (2) application	C_{t2}	Uniform distribution (1.45; 2)	
costs laboratory analysis (ELISA), second (2) test	C_{ELI2}	Fixed value (15)	
Indirect Costs incurred by antigen analysis (direct detection) by blood sampling per year in each scenario	$ICdidb_{y,s}$	$ICdidb_{y,s} = (n_{dby,s} * C_{db}) + (n_{fdb_{y,s}} * C_{fb})$	
number of animals tested (direct detection) by blood (antigen)	$n_{dby,s}$		calculated in the DSM
Costs direct detection by blood (antigen) per animal	C_{db}	$C_{db} = c_{bs} + c_{PCR}$	
Costs blood sampling	C_{bs}	Triangle distribution (3;7;10)	According to the official scale of fees for veterinarians (Gebührenordnung für Tierärzte)
Costs laboratory analysis (PCR)	C_{PCR}	Triangle distribution (5;8;11)	

number of farms sampled (for direct detection in blood samples)	$n_{fdb_{y,s}}$		calculated in the DSM
Costs per farm for blood sampling	C_{fb}	$C_{fb} = c_{hf} + c_s + c_{sh} + c_c$	
costs herd fee	C_{hf}	Triangle distribution (17;19;23)	Herd fee charged for blood sampling by veterinarians are ... Euros per callout and includes travel costs and veterinary advice
costs sample handling	C_s	Fixed (2)	
costs sample shipping	C_{sh}	Triangle distribution (0.1; 0.2; 0.5)	
costs communication of the test result	C_c	Triangle distribution (0.2; 0.4; 0.8)	
Indirect Costs incurred by antibody testing (indirect detection) by blood sampling per year in each scenario	$IC_{indb_{y,s}}$	$IC_{indb_{y,s}} = (n_{iby,s} * C_{ib}) + (n_{fiby,s} * C_{fb})$	
number of animals tested (indirect detection) by blood (antibodies)	$n_{iby,s}$		calculated in the DSM
Costs antibody testing (indirect detection) by blood per animal	C_{ib}	$C_{ib} = c_{bs} + c_{ELISA}$	
costs laboratory analysis (ELISA)	C_{ELISA}	Triangle distribution (8; 9; 10)	
number of farms sampled (for indirect detection in blood)	$n_{fiby,s}$		calculated in the DSM
Indirect Costs incurred by vaccination per year in each scenario	$IC_{va_{y,s}}$	$IC_{va_{y,s}} = (n_{vafy,s} * C_{vaf}) + (n_{vaiy,s} * n_{vi} * c_{va} + c_{vacc})$	
number of vaccinated farms	$n_{vafy,s}$		calculated in the DSM
Costs for vaccination, farm level	C_{vaf}	$C_{vaf} = c_{hf}$	Herd fee charged for vaccination by veterinarians are ... Euros per callout and includes travel costs and veterinary advice
number of vaccinated animals	$n_{vaiy,s}$		calculated in the DSM
number of vaccinations (immunisations) per animal	n_{vi}	Triangle distribution (1.2;1.25;1.33)	
costs for one vaccine	C_{va}	Triangle distribution (3;4;5)	Vaccine: (Pape, 2000)
costs for vaccinating one animal	C_{vacc}	Triangle distribution (1;1.4;1.8)	
Indirect Costs incurred by preventive slaughter of PIs per year in each scenario	$IC_{ps_{y,s}}$	$IC_{ps_{y,s}} = (nsPIC_{y,s} * v_{PIC}) + (nsPII_{y,s} * v_{PII}) + (nsPIC_{y,s} * v_{PIC})$	

number of preventively slaughtered PI calves (0-6 months), young cattle (6-24 months), cows (>24 months)	nsPIC _{y,s} nsPIy _{y,s} nsPIC _{y,s}		calculated in the DSM
compensation (value) for preventive slaughtering a PI calf	V _{PIc}	Uniform distribution (18;75)	Based on the compensation for preventive slaughtering (“Merzungsbeihilfe”) provided by the animal health insurances (Tierseuchenkassen). Compensation depends among other factors, on the breed, gender and age of the animal.
Compensation (value) for preventive slaughtering a PI young cattle	V _{PIy}	Uniform distribution (3;150)	
Compensation (value) for preventive slaughtering a PI Cow	V _{PIc}	Uniform distribution (150;400)	
Indirect Costs incurred by trade restrictions per year in each scenario	IC _{Tr_{y,s}}	Triangular distribution (100;115;118)	Based on (Anonymus, 2016), we assumed that within 40 days of quarantine, each affected farm would want to move <u>three pregnant and three non-pregnant animals</u> . This implies the following costs for three pregnant and three non-pregnant animals respectively: travel 10 €, taking blood samples 10 €, handling and shipping samples 9 €, laboratory analysis 30 € (3x10 €). Hence, the movement ban would result in 118 € (2x59 €) additional veterinary costs per affected premise.

Anonymus, 2001. Position paper of the EU Thematic network on control of bovine viral diarrhoea virus (BVDV).

Anonymus, 2010. Antwort auf die Kleine Anfrage Drucksache 17/3263 Ohrstanz-Gewebeprobe bei Rindern im Rahmen der BVD-Impfung.

Anonymus, 2016. Zweite Verordnung zur Änderung der BVDV-Verordnung. Drucksache 200/16 vom 20.04.16.

Burgstaller, J., Obritzhauser, W., Kuchling, S., Kopacka, I., Pinior, B., Köfer, J., 2016. The effect of bovine viral diarrhoea virus on fertility in dairy cows: two case-control studies in the province of Styria, Austria. Berl Münch Tierärztl Wochenschr 129, 103-110.

Pape, K.-R., 2000. BVD-Bekämpfung: Worüber die Experten streiten. Top agrar 6, 18-21.

Viet, A.F., Fourichon, C., Seegers, H., Jacob, C., Guihenneuc-Jouyaux, C., 2004. A model of the spread of the bovine viral-diarrhoea virus within a dairy herd. Prev Vet Med 63, 211-236.

Table S4: Equations used in the benefit-cost analysis

Parameter	Notation	Equation
Benefit-Cost Ratio in each scenario	BCR_s	$BCR_s = \frac{\sum_{y=2011}^{2030} B_{y,s}}{\sum_{y=2011}^{2030} IC_{y,s}}$
Present Value Benefit	PVB_s	$PVB_s = \sum_{y=2011}^{2030} \frac{B_{y,s}}{(1+r)^{(y-2011)}}$
Benefit per year	$B_{y,s}$	$B_{y,s} = DC_{y,s1} - DC_{y,s}$
Interest rate	r	$r = 3\%$
Present Value Indirect Costs	$PVIC_s$	$PVIC_s = \sum_{y=2011}^{2030} \frac{IC_{y,s}}{(1+r)^{(y-2011)}}$
Net value	NV_s	$NV_s = \sum_{y=2011}^{2030} B_{y,s} - \sum_{y=2011}^{2030} IC_{y,s}$
Net present value	NPV_s	$NPV_s = \sum_{y=2011}^{2030} \frac{B_{y,s}}{(1+r)^{(y-2011)}} - \sum_{y=2011}^{2030} \frac{IC_{y,s}}{(1+r)^{(y-2011)}}$

Table S5: Probability of transient BVDV infections per pregnancy stage (and overall probability).

effect	Pregnancy stage				Post partum
	days 0 - 70	days 71 - 120	days 121 - 180	days 181 - 285	days 286 - 385
birth of a PI calf	0.90 (0.16)	0.45 (0.06)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
abortion. stillbirth	0.10 (0.02)	0.15 (0.02)	0.20 (0.03)	0.05 (0.01)	0.00 (0.00)
congenital defects. growth retardation	0.00 (0.00)	0.15 (0.02)	0.25 (0.04)	0.15 (0.04)	0.00 (0.00)
Immune	0.00 (0.00)	0.25 (0.03)	0.55 (0.09)	0.80 (0.22)	0.00 (0.00)
no effect	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	1.00 (0.26)
total	1.00 (0.18)	1.00 (0.13)	1.00 (0.16)	1.00 (0.27)	1.00 (0.26)

Table S6: Prolongation of the calving interval (Ci) due to a transient BVDV infection on the foetus

	days 0 - 70	days 71 - 120	days 121 - 180	days 181 - 285	days 286 - 385	total average prolongation of the Ci (days)
average prolongation of the Ci (days)	35	95	150	233	335	
probability of outcome of abortion. stillbirth (see table S5)	0.02	0.02	0.03	0.01	0.00	
prolongation of the Ci (days)	0.64	1.85	4.68	3.17	0.00	10.33

Table S7: Results of the economic model: Mean total costs (million Euros), thereof direct and indirect costs (million Euros).

scenario	costs	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
sc1	total costs	129	129	132	122	122	120	118	117	117	115	113	108	106	105	103	104	99	100	100	100
	direct costs	129	129	132	122	122	120	118	117	117	115	113	108	106	105	103	104	99	100	100	100
sc 2	total costs	195	146	117	109	99	92	87	86	87	88	86	84	83	82	82	82	83	82	81	80
	direct costs	105	55	31	26	19	14	11	10	11	11	9	8	7	6	6	7	7	6	5	5
	indirect costs	91	91	86	83	80	78	77	76	76	77	76	76	76	76	76	75	76	76	75	75
sc 3	total costs	195	146	117	109	99	91	87	86	87	86	85	83	81	81	81	79	79	80	79	79
	direct costs	105	55	31	26	19	13	10	10	10	10	9	7	6	5	5	4	4	4	4	4
	indirect costs	90	91	86	83	80	78	77	76	76	77	76	76	75	75	75	75	75	75	75	75
sc 4	total costs	195	146	117	108	99	91	79	53	78	71	46	37	39	39	36	35	36	38	35	36
	direct costs	104	56	31	26	19	13	17	53	78	71	46	37	39	39	36	35	36	38	35	36
	indirect costs	90	90	86	83	80	78	62	0	0	0	0	0	0	0	0	0	0	0	0	0
sc 5	total costs	195	146	117	109	99	92	87	92	109	118	125	132	137	138	138	138	138	138	139	138
	direct costs	105	55	31	26	19	13	10	10	10	5	1	0	0	0	0	0	0	0	0	0
	indirect costs	91	91	86	83	80	78	77	82	99	113	123	132	137	138	138	138	138	139	138	138
sc 6	total costs	195	147	118	109	99	91	89	310	283	256	238	221	209	200	195	190	184	177	174	171
	direct costs	104	56	32	26	19	13	12	10	11	11	11	10	8	7	6	6	5	5	4	5
	indirect costs	91	91	86	83	80	78	77	300	272	244	227	211	201	193	189	184	179	172	170	166
sc 7	total costs	195	146	118	109	99	92	89	178	162	152	141	130	122	119	116	113	112	109	105	104
	direct costs	104	56	32	26	19	13	12	10	10	11	11	9	7	6	6	6	6	5	4	4
	indirect costs	91	91	86	83	80	78	77	168	152	141	130	121	115	113	110	108	107	104	101	100
sc 8	total costs	195	146	117	109	99	91	87	297	378	437	491	516	527	534	533	534	533	535	535	534
	direct costs	104	56	31	26	19	13	10	10	8	3	1	0	0	0	0	0	0	0	0	0
	indirect costs	90	90	86	83	80	78	77	287	370	433	491	516	527	534	533	534	533	535	535	534
sc 9	total costs	195	146	118	109	99	91	85	116	124	131	138	146	150	151	151	151	151	151	151	151
	direct costs	105	55	31	26	19	13	9	10	8	3	1	0	0	0	0	0	0	0	0	0
	indirect costs	90	91	86	83	80	78	76	106	116	127	137	145	150	151	151	151	151	151	151	151
sc 10	total costs	195	146	117	109	99	91	56	243	222	183	150	134	134	136	130	116	106	105	105	104
	direct costs	104	56	31	26	19	13	14	26	32	18	8	6	10	14	13	8	5	6	8	9

scenario	costs	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
	indirect costs	91	91	86	83	80	78	42	217	190	165	142	128	124	122	117	108	101	99	96	95
sc 11	total costs	194	146	117	109	99	91	58	55	94	99	84	81	82	81	76	72	71	69	68	66
	direct costs	104	55	31	26	19	13	16	50	71	62	36	23	19	18	13	8	7	5	4	3
	indirect costs	91	91	86	83	80	78	42	5	23	37	49	58	63	64	63	63	63	64	64	63
sc 12	total costs	194	145	117	108	99	91	87	59	63	81	84	76	78	75	73	70	68	67	66	65
	direct costs	104	56	31	26	19	13	10	15	41	44	36	19	15	12	10	7	5	4	3	2
	indirect costs	90	90	86	83	80	78	77	44	22	37	48	57	62	63	63	63	63	63	63	63
sc 13	total costs	195	146	117	109	99	91	54	62	142	155	153	156	158	159	159	158	158	159	158	158
	direct costs	104	56	31	26	19	13	11	16	27	16	4	1	0	0	0	0	0	0	0	0
	indirect costs	90	90	86	83	80	78	43	47	115	139	149	155	158	159	159	158	158	159	158	158