

Supplemental Online Content

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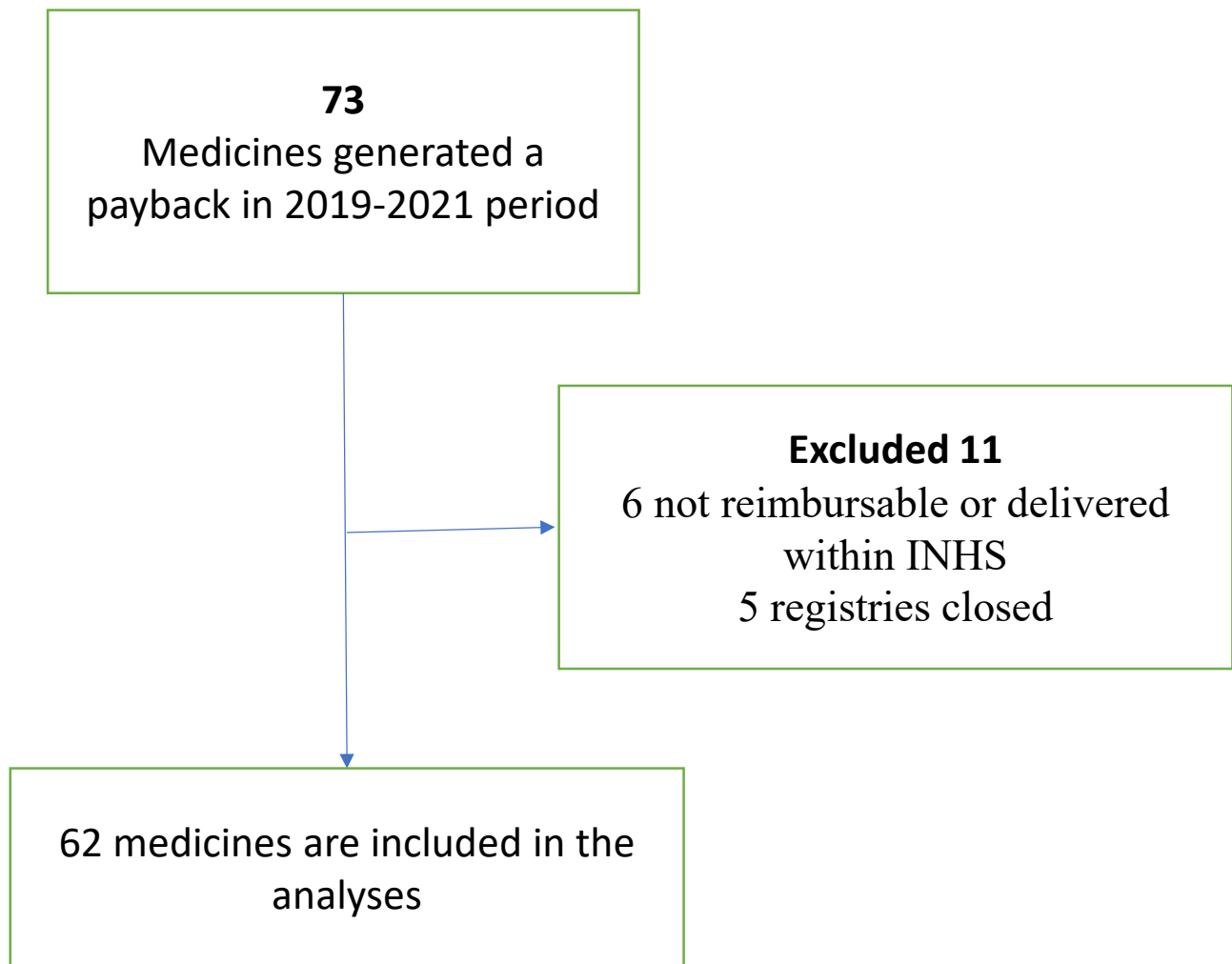
This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Medicine included in the analysis (n=62)

ATC	Active ingredient
L01CD01	PACLITAXEL
L01FX05	BRENTUXIMAB VEDOTIN
L01EG02	EVEROLIMUS
L01ED03	ALECTINIB
L01BA04	PEMETREXED
L01FG01	BEVACIZUMAB
L01FX07	BLINATUMOMAB
L01EA04	BOSUTINIB
L01EX04	VANDETANIB
L01EE02	COBIMETINIB
M05BX05	BUROSUMAB
L01FG02	RAMUCIRUMAB
L01BC08	DECITABINA
L01FC01	DARATUMUMAB
J05AP55	SOFOSBUVIR/VELPATASVIR
L01FE01	CETUXIMAB
L01XJ01	VISMODEGIB
L01FA03	OBINUTUZUMAB
L01EB03	AFATINIB
L01XX41	ERIBULINA
L01FD01	TRASTUZUMAB
L04AB04	ADALIMUMAB
L01EA05	PONATINIB
L01EK01	AXITINIB
L01EB01	GEFITINIB
L01EJ01	RUXOLITINIB
L01CA05	VINFLUNINA
L01FD03	TRASTUZUMAB EMTANSINE
L01XG02	CARFILZOMIB
S01LA04	RANIBIZUMAB
J05AP57	GLECAPREVIR/PIBRENTASVIR
L01EE01	TRAMETINIB
L03AX16	PLERIXAFOR
L01EX02	SORAFENIB
L01FF01	NIVOLUMAB
L04AX04	LENALIDOMIDE
N02BG10	DELTA-9-TETRAIDROCANNABINOLO/CANNABIDIOLO
H01CB05	PASIREOTIDE
L04AB06	GOLIMUMAB
J04AK05	BEDAQUILINA
L01EA02	DASATINIB
L01EX01	SUNITINIB
L01EC02	DABRAFENIB
L01EB04	OSIMERTINIB

L01EB02	ERLOTINIB
L01EA03	NILOTINIB
L01EH01	LAPATINIB
L01EX09	NINTEDANIB
L01FE02	PANITUMUMAB
L01XG01	BORTEZOMIB
L01BC07	AZACITIDINA
J05AP56	SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR
L01EX03	PAZOPANIB
L01ED01	CRIZOTINIB
L02BB04	ENZALUTAMIDE
L01FX04	IPILIMUMAB
L01CX01	TRABECTEDINA
L01XX44	AFLIBERCEPT
L01EC01	VEMURAFENIB
J05AP54	ELBASVIR/GRAZOPREVIR
L01ED02	CERITINIB
L02BX03	ABIRATERONE

eFigure 1A. Flow-chart of medicines included in the analysis



eFigure 1B. Distribution of medicines included in the analysis by ATC I

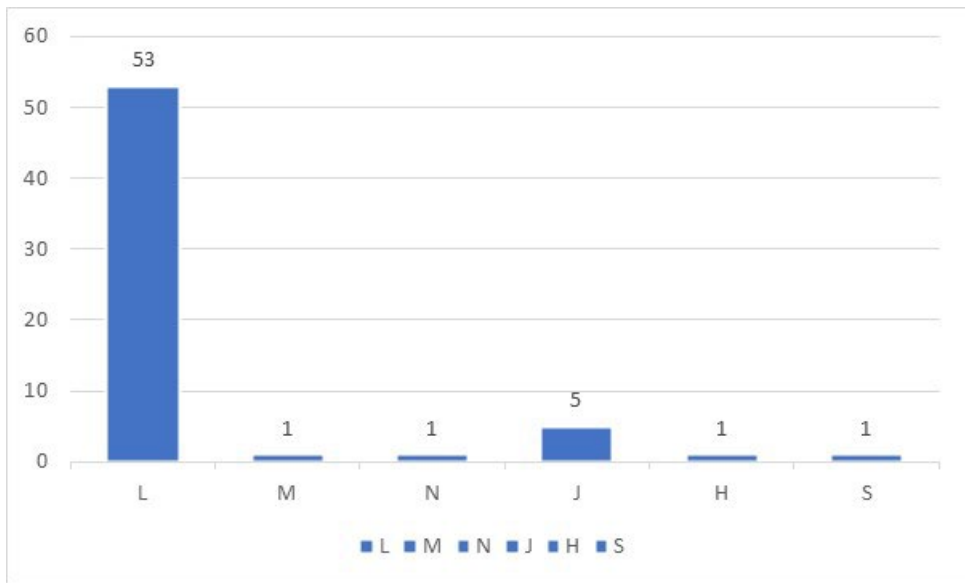
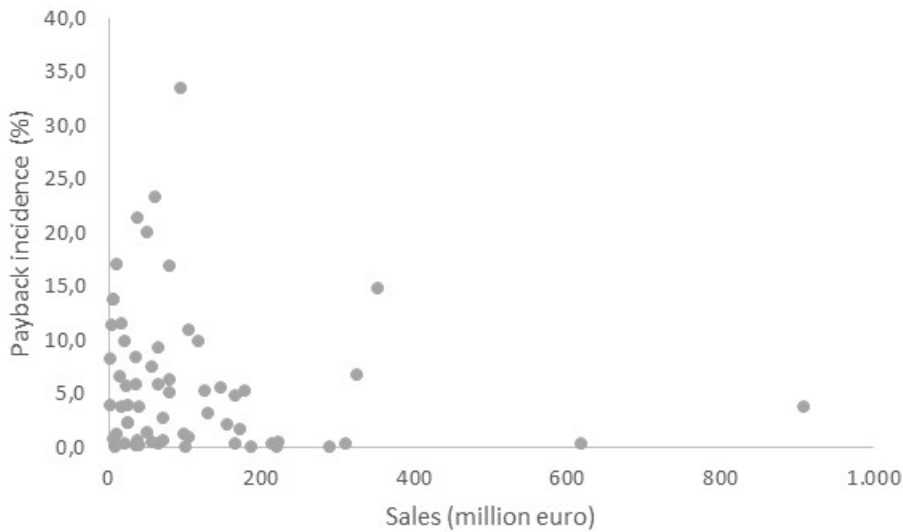


Table e2. Number of medicinal products, amount of payback and payback share by type and category of agreement in 2019-2021; only medicine with expenditure data by indication were included.

Type of agreement/category	Number of medicinal products	Pay-back 2019-2021 (euro)	Payback % on expenditure (median)
MEA Outcome-based	3	15.480.784,3	4,8%
Payment by result	3	15.480.784,3	4,8%
MEA Financia- based	4	26.141.791,9	2,0%
Cost-sharing	3	13.437.402,2	1,2%
Capping	1	12.704.389,7	5,9%
Total	7	41.622.576,3	2,6%

Medicines included: dabrafenib, trametinib, osimertinib, daratumumab, elbasvir/grazoprevir, alectinib, glecaprevir/pibrentasvir

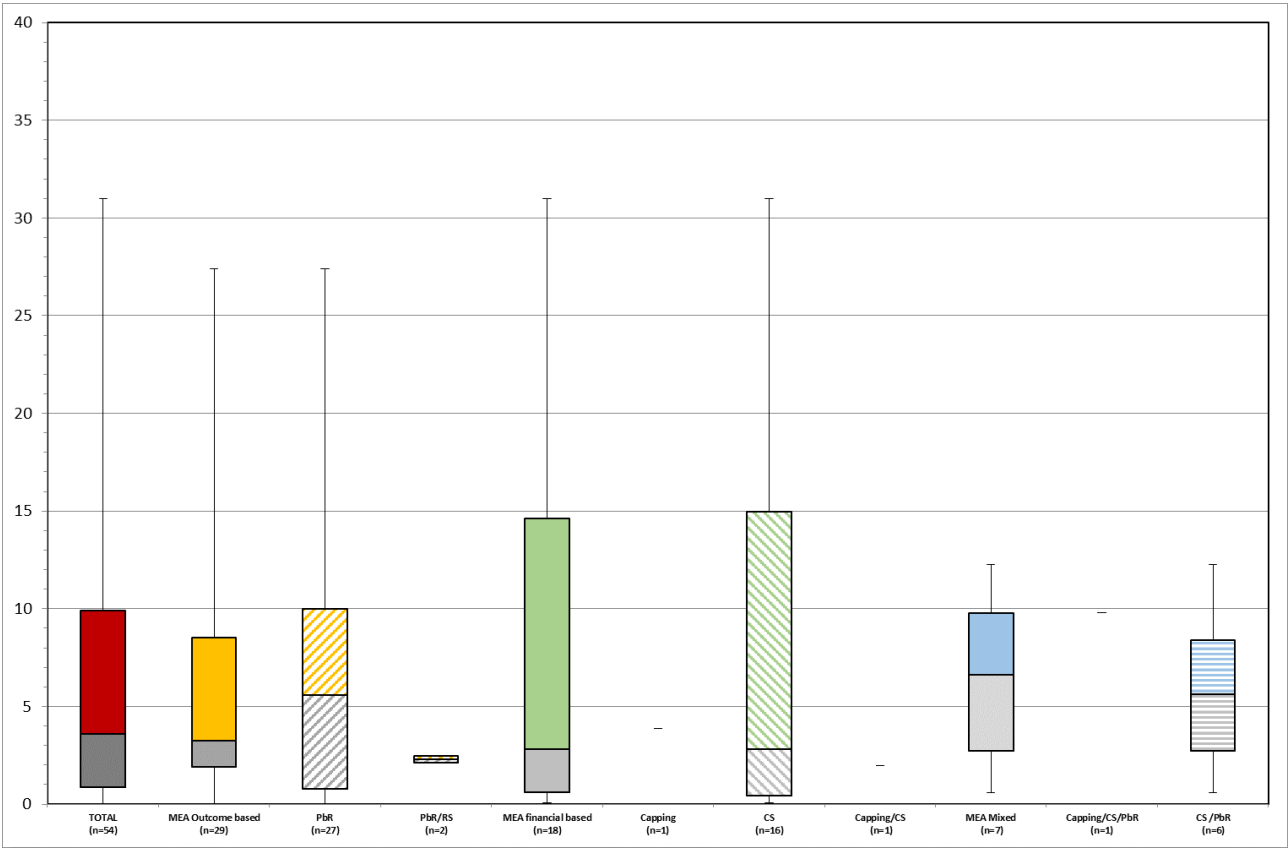
eFigure 2. Relation between payback share and INHS expenditure 2019-2021



eTable 3. Number of medicinal products, overall expenditure, amount of payback and payback share on expenditure by type and category of agreement in 2019

Type of agreement/Category	Number of medicinal products N(%)	Overall expenditure 2019 (euro)	Pay-back 2019 euro (%)	Payback % on expenditure (median)
MEA financial-based	18 (33.3%)	1.035.967.871	35.038.878 (34.1%)	2.8
Capping	1 (1.9%)	124.724.901	4.824.632 (4.7%)	3.9
Capping/Cost-sharing	1 (1.9%)	34.680.808	677.947 (0.7%)	2.0
Cost-sharing	16 (29.6%)	876.562.162	29.536.299 (28.8%)	2.8
MEA Outcome-based	29 (53.7%)	817.799.783	29.573.429 (28.8%)	3.3
Payment by result /Risk-sharing	2 (3.7%)	69.520.191	1.586.187 (1.5%)	2.3
Payment by result	27 (50.0%)	748.279.592	27.987.242 (27.3%)	5.6
MEA mixed	7 (13.0%)	410.344.022	38.040.817 (37.1%)	6.6
Capping/Cost-sharing/Payment by result	1 (1.9%)	193.554.392	18.955.376 (18.5%)	9.8
Cost-sharing /Payment by result	6 (11.1%)	216.789.629	19.085.441 (18.6%)	5.6
TOTAL	54 (100%)	2.264.111.678	102.653.124 (100%)	3.6

eFigure 3. Box plot: share of pay-back on expenditure by type and category of agreement: year 2019



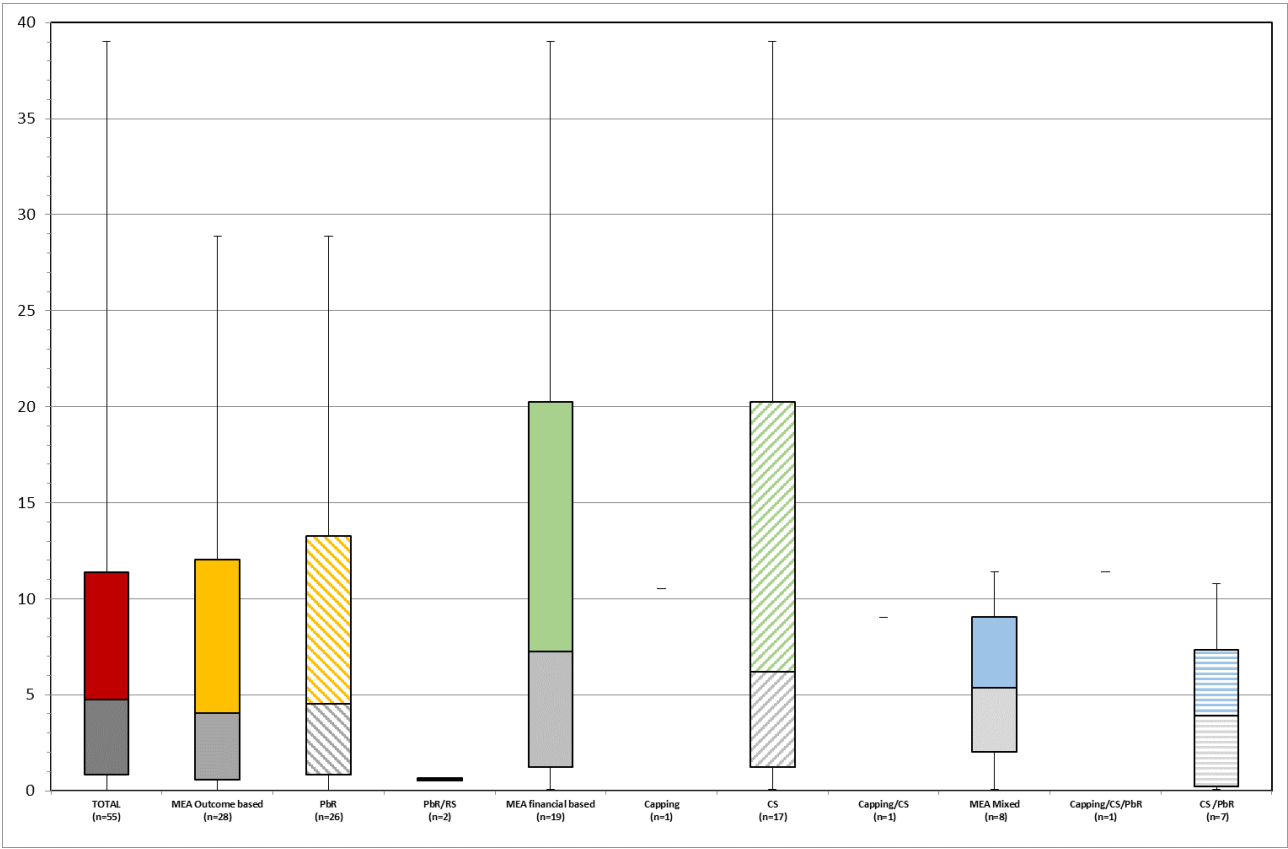
PbR: Payment by Result RS: Risk sharing CS: Cost-sharing

Note: The line splitting the box in two represents the median value. The lower edge of the box represents the lower quartile. The upper edge of the box shows the upper quartile; at the end of the whiskers the minimum and maximum values are represented.

eTable 4. Number of medicinal products, overall expenditure, amount of payback and payback share on expenditure by type and category of agreement in 2020

Type of agreement/Category	Number of medicinal products N (%)	Overall expenditure 2020 (Euro)	Pay-back 2020 Euro (%)	Payback Incidence% on expenditure (median)
MEA Financial based	19 (34.5%)	1.128.751.829	49.880.408 (47.6%)	7.3
Capping	1 (1.8%)	50.155.251	5.282.003 (5.0%)	10.5
Capping/Cost-sharing	1 (1.8%)	35.739.042	3.228.698 (3.1%)	9.0
Cost-sharing	17 (30.9%)	1.042.857.535	41.369.706 (39.5%)	6.2
MEA Outcome based	28 (50.9%)	786.208.625	28.734.949 (27.4%)	4.1
Payment by result	26 (47.3%)	717.120.223	28.329.842 (27.0%)	4.5
Payment by result /Risk-sharing	2 (3.6%)	69.088.402	405.106,53 (0.4%)	0.6
MEA Mixed	8 (14.5%)	414.037.568	26.130.517 (24.9%)	5.3
Capping/Cost-sharing/Payment by result	1 (1.8%)	131.902.657	15.023.828 (14.3%)	11.4
Cost-sharing /Payment by result	7 (12.7%)	282.134.911	11.106.689 (10.6%)	3.9
TOTAL	55 (100.0%)	2.328.998.021	104.745.874,45 (100.0%)	4.7

eFigure 4. Box plot: distribution of the magnitude of paybacks shown as share of total expenditures, by type and category of agreement: year 2020



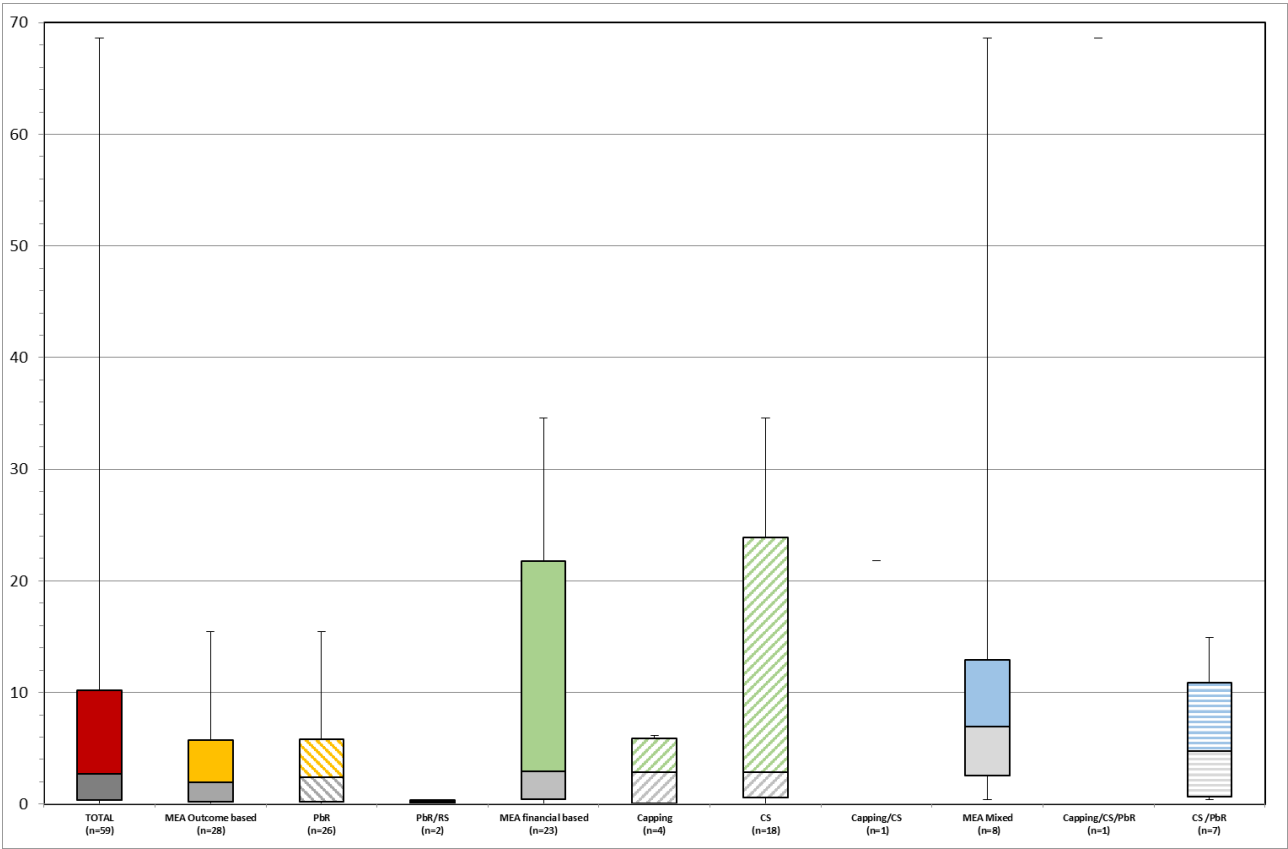
PbR: Payment by Result RS: Risk sharing CS: Cost-sharing

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eTable 5. Number of medicinal products, overall expenditure, amount of payback and payback share on expenditure by type and category of agreement in 2021

Type of agreement/Category	Number of medicinal products N (%)	Overall expenditure (euro)	Pay-back 2021 euro (%)	Payback % on expenditure (median)
MEA Financial-based	23 (39.0%)	1.412.619.200	73.314.921 (61.1%)	3.0
Capping	4 (6.8%)	93.819.60	3.266.989 (2.7%)	2.9
Capping/Cost-sharing	1 (1.7%)	34.648.778	7.542.714 (6.3%)	21.8
Cost-sharing	18 (30.5%)	1.284.150.815	62.505.218 (52.0%)	2.8
MEA Outcome-based	28 (47.5%)	742.382.823	16.185.949 (13.5%)	2.0
Payment by result	26 (44.1%)	675.835.448	16.035.020 (13.4%)	2.4
Payment by result /Risk-sharing	2 (3.4%)	66.547.375	150.929 (0.1%)	0.2
MEA Mixed	8 (13.6%)	291.782.443	30.611.101 (25.5%)	6.9
Cost-sharing /Payment by result	7 (11.9%)	265.665.965	12.692.599 (10.6%)	4.7
Capping/Cost-sharing /Payment by result	1 (1.7%)	26.116.478	17.918.502 (14.9%)	68.6
TOTAL	59 (100.0%)	2.446.784.466	120.111.971 (100.0%)	2.7

eFigure 5. Box plot: distribution of the magnitude of paybacks shown as share of total expenditures, by type and category of agreement: year 2021



Note: The line splitting the box in two represents the median value. The lower edge of the box represents the lower quartile. The upper edge of the box shows the upper quartile; at the end of the whiskers the minimum and maximum values are represented.