**Appendix 2** Clinical outcomes and overall costs of treatment strategies

**TABLE 1.** Clinical outcomes and cost of consequences of oral ibuprofen, intravenous (IV) indomethacin, and IV ibuprofen. (Ibuprofen versus indomethacin model)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| PDA treatment strategy | Outcome event | Cost of health state, QAR (USD) | Proportional cost of health state, QAR (USD) | Average cost per outcome category, QAR (USD) | Total average cost of oral ibuprofen, QAR (95% CI) (USD [95% CI]) |
| Oral ibuprofen | **Success** |  |  | 373,915 (102,724) | 414,760  (413,529- 415,994)  (113, 945 [113,607- 114,284]) |
|  | PDA closure without adverse events | 358,467 (98,480) | 192,717 (52,944.3) |  |  |
|  | PDA closure with PVL | 467,447 (128,419.6) | 46,087 (12,661.2) |  |  |
|  | PDA closure with ROP | 450,167 (123,672.3) | 32,402 (8,901.7) |  |  |
|  | PDA closure with BPD | 529,221 (145,390.4) | 102,708 (28,216.5) |  |  |
|  | **Failure** |  |  | 40,848 (11,222) |  |
|  | No response to first course with second course | 437,685 (120,243) | 4,805 (1,320) |  |  |
|  | No response to first course with surgical ligation | 659,495 (181,180) | 3,453 (949) |  |  |
|  | Death | 358,467 (98,480) | 5,574 (1,531) |  |  |
|  | Premature discontinuation with pulmonary hemorrhage | 428,190 (117,635) | 576 (158) |  |  |
|  | Premature discontinuation with IVH | 431,961 (118,671) | 7,390 (2,030) |  |  |
|  | Premature discontinuation with NEC | 457,341 (125,643) | 3,112 (855) |  |  |
|  | Premature discontinuation with GIB | 399,504 (109,754) | 14,411(3,959) |  |  |
|  | Premature discontinuation with intestinal perforation | 458,451 (125,948) | 1,263 (347) |  |  |
|  | Premature discontinuation with oliguria | 342,599 (94,121) | 264 (73) |  |  |
| PDA treatment strategy | **Outcome event** | **Cost of health state, QAR (USD)** | **Proportional cost of health state, QAR (USD)** | **Average cost per outcome category, QAR (USD)** | **Total average cost of oral ibuprofen, QAR (95% CI) (USD [95% CI])** |
| IV indomethacin | **Success** |  |  | 327,228 (89,898) | QAR 436,159 (434,762- 437,553) (119,824 [119,440-120,207]) |
|  | PDA closure without adverse events | 365,126 (100,309) | 128,186 (35,216.) |  |  |
|  | PDA closure with PVL | 474,106 (130,249) | 20,640 (5,670.) |  |  |
|  | PDA closure with ROP | 456, 826 (125) | 83,813 (23,026) |  |  |
|  | PDA closure with BPD | 535,880 (147,220) | 94,589 (25,986) |  |  |
|  | **Failure** |  |  | 108,930 (29,926) |  |
|  | No response to first course with second course | 453,223 (124,512) | 17,605 (4,837) |  |  |
|  | No response to first course with surgical ligation | 666,154 (183,009) | 18,717 (5,142) |  |  |
|  | Death | 365,126 (100,309) | 12,674 (3,482) |  |  |
|  | Premature discontinuation with pulmonary hemorrhage | 432,628 (118,854) | 6,241 (1,715) |  |  |
|  | Premature discontinuation with IVH | 436,400 (119,890) | 10,393 (2,855) |  |  |
|  | Premature discontinuation with NEC | 461,780 (126,863) | 8,548 (2,348) |  |  |
|  | Premature discontinuation with GIB | 403,943 (110,973) | 10,708 (2,942) |  |  |
|  | Premature discontinuation with intestinal perforation | 462,890 (127,168) | 12,180 (3,346) |  |  |
|  | Premature discontinuation with oliguria | 347,038 (95,340) | 11,864 (3,259) |  |  |
| PDA treatment strategy | **Outcome event** | **Cost of health state, QAR (USD)** | **Proportional cost of health state, QAR (USD)** | **Average cost per outcome category, QAR (USD)** | **Total average cost of oral ibuprofen, QAR (95% CI) (USD [95% CI])** |
| IV ibuprofen | **Success** |  |  | 313,015 (85,993) | 435,795  (434,427- 437,164)  (119,724 [119,348-120,100]) |
|  | PDA closure without adverse events | 360,677 (99,087) | 122,794 (33,735) |  |  |
|  | PDA closure with PVL | 469,657 (129,027) | 26,149 (7,184) |  |  |
|  | PDA closure with ROP | 452,377 (124,280) | 63,049 (17,321) |  |  |
|  | PDA closure with BPD | 531,431 (145,997.6) | 101,024 (27,754) |  |  |
|  | **Failure** |  |  | 122,779 (33,731) |  |
|  | No response to first course with second course | 442,105 (121,457) | 28,142 (7,731) |  |  |
|  | No response to first course with surgical ligation | 661,705 (181,787) | 21,706 (5,963) |  |  |
|  | Death | 360,677 (99,087) | 15,277.4 (4,197.1) |  |  |
|  | Premature discontinuation with pulmonary hemorrhage | 429,846 (118,090) | 9,338 (2,565) |  |  |
|  | Premature discontinuation with IVH | 433,619 (119,126) | 15,551 (4,272) |  |  |
|  | Premature discontinuation with NEC | 458,999 (126,099) | 8,210 (2,256) |  |  |
|  | Premature discontinuation with GIB | 401,161 (110,209) | 11,320 (3,110) |  |  |
|  | Premature discontinuation with intestinal perforation | 460,109 (126,403) | 8,958 (2,461) |  |  |
|  | Premature discontinuation with oliguria | 344,256 (94,576) | 4,278 (1,175) |  |  |
| PDA patent ductus arteriosus, CI confidence interval, QAR Qatari Riyal, USD United States dollar, PVL periventricular leukomalacia, ROP retinopathy of prematurity, BPD bronchopulmonary dysplasia, IVH intraventricular hemorrhage, NEC necrotizing enterocolitis, GIB gastrointestinal bleeding | | | | | |

**TABLE 2.** Clinical and economic outcomes of oral ibuprofen, oral paracetamol, and intravenous ibuprofen. (Ibuprofen versus paracetamol model)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| PDA treatment strategy | Outcome event | Cost of health state, QAR (USD) | Proportional cost of health state, QAR (USD) | Average cost per outcome category, QAR (USD) | Total average cost of oral ibuprofen, QAR (95% CI) (USD [95% CI]) |
| Oral ibuprofen | **Success** |  |  | 246,362 (67,682) | 404,972  (403,774-406,166) (111,256 [110,927-111,584]) |
|  | PDA closure without adverse events | 358,467 (98,480) | 157,644 (43,309) |  |  |
|  | PDA closure with PVL | 467,447 (128,420) | 15,281 (4,198) |  |  |
|  | PDA closure with ROP | 450,167 (123,672) | 43,820 (12,039) |  |  |
|  | PDA closure with BPD | 529,221 (145,390) | 29,617 (8,137) |  |  |
|  | **Failure** |  |  | 158,609 (43,574) |  |
|  | No response to first course with second course | 437,685 (120,243) | 61,475 (16,889) |  |  |
|  | No response to first course with surgical ligation | 659,495 (181,180) | 14,530 (3,992) |  |  |
|  | Death | 358,467 (98,480) | 23,760 (6,528) |  |  |
|  | Premature discontinuation with pulmonary hemorrhage | 428,190 (118,671) | 13,415 (3,685) |  |  |
|  | Premature discontinuation with IVH | 431,961 (118,671) | 6,817 (1,873) |  |  |
|  | Premature discontinuation with NEC | 457,341 (125,643) | 10,680 (2,934) |  |  |
|  | Premature discontinuation with GIB | 399,504 (109,754) | 14,081 (3,868) |  |  |
|  | Premature discontinuation with intestinal perforation | 458,451 (125,948) | 913 (251) |  |  |
|  | Premature discontinuation with oliguria | 342,599 (94,121) | 12,938 (3,554) |  |  |
| PDA treatment strategy | **Outcome event** | **Cost of health state, QAR (USD)** | **Proportional cost of health state, QAR (USD)** | **Average cost per outcome category, QAR (USD)** | **Total average cost of oral ibuprofen, QAR (95% CI) (USD [95% CI])** |
| Oral paracetamol | **Success** |  |  | 242,045 (66,496) | 397,798  (396,571-399,024) (109,285 [108, 948-109,622]) |
|  | PDA closure without adverse events | 358,468 (98,480) | 183,442 (50,396) |  |  |
|  | PDA closure with PVL | 467,449 (128,420) | 15,449 (4,244) |  |  |
|  | PDA closure with ROP | 450,169 (123,673) | 19,050 (5,234) |  |  |
|  | PDA closure with BPD | 529,222 (145,391) | 24,104 (6,622) |  |  |
|  | **Failure** |  |  | 155,752 (42,789) |  |
|  | No response to first course with second course | 437,687 (120,244) | 73,126 (20,090) |  |  |
|  | No response to first course with surgical ligation | 659,410 (181,157) | 9,192.4 (2,525) |  |  |
|  | Death | 358,468 (98,480) | 26,009 (7,145) |  |  |
|  | Premature discontinuation with pulmonary hemorrhage | 428,191 (117,635) | 13,950 (3,833) |  |  |
|  | Premature discontinuation with IVH | 431,963 (118,671) | 7,775 (2,136) |  |  |
|  | Premature discontinuation with NEC | 457,082 (125,572) | 13,255 (3,642) |  |  |
|  | Premature discontinuation with GIB | 399,505 (109,754) | 5,593 (1,537) |  |  |
|  | Premature discontinuation with intestinal perforation | 458,453 (125,949) | 0 (0) |  |  |
|  | Premature discontinuation with oliguria | 342,600 (94,121) | 6,852 (1,882) |  |  |
| PDA treatment strategy | **Outcome event** | **Cost of health state, QAR (USD)** | **Proportional cost of health state, QAR (USD)** | **Average cost per outcome category, QAR (USD)** | **Total average cost of oral ibuprofen, QAR (95% CI) (USD [95% CI])** |
| IV ibuprofen | **Success** |  |  | 192,574 (52,905) | 415,589  (414,257-416,921)  (114,173 [113,807-114,539]) |
|  | PDA closure without adverse events | 360,677 (99,087) | 97,614 (26,817) |  |  |
|  | PDA closure with PVL | 469,657 (129,027) | 11,547 (3,172) |  |  |
|  | PDA closure with ROP | 452,377 (124,280) | 56,134 (15,421) |  |  |
|  | PDA closure with BPD | 531,431 (145,998) | 27,278 (7,494) |  |  |
|  | **Failure** |  |  | 223,015 (61,268) |  |
|  | No response to first course with second course | 442,105 (121,457) | 80,636 (22,153) |  |  |
|  | No response to first course with surgical ligation | 661,705 (181,787) | 20,455 (5,620) |  |  |
|  | Death | 360,677 (99,087) | 14,368 (3,947) |  |  |
|  | Premature discontinuation with pulmonary hemorrhage | 429,847 (118,090) | 47,984 (13,183) |  |  |
|  | Premature discontinuation with IVH | 433,619 (119,126) | 3,165 (870) |  |  |
|  | Premature discontinuation with NEC | 458,999 (126,099) | 6,218 (1,708) |  |  |
|  | Premature discontinuation with GIB | 401,161 (110,209) | 2,441 (671) |  |  |
|  | Premature discontinuation with intestinal perforation | 460,109 (126,403) | 1,428 (392) |  |  |
|  | Premature discontinuation with oliguria | 344,256 (94,576) | 46,321 (12,726) |  |  |
| |  | | --- | | PDA patent ductus arteriosus, CI confidence interval, QAR Qatari Riyal, USD United States dollar, PVL periventricular leukomalacia, ROP retinopathy of prematurity, BPD bronchopulmonary dysplasia, IVH intraventricular hemorrhage, NEC necrotizing enterocolitis, GIB gastrointestinal bleeding |   . | | | | | |

**FIG 1.** The relative value of cost components for each of the study drugs (ibuprofen versus indomethacin model). QAR: Qatari riyal, IV: intravenous

**Fig. 2** The relative value of cost components for each of the study drugs (ibuprofen versus paracetamol model). QAR: Qatari riyal, IV: intravenous, PO: oral