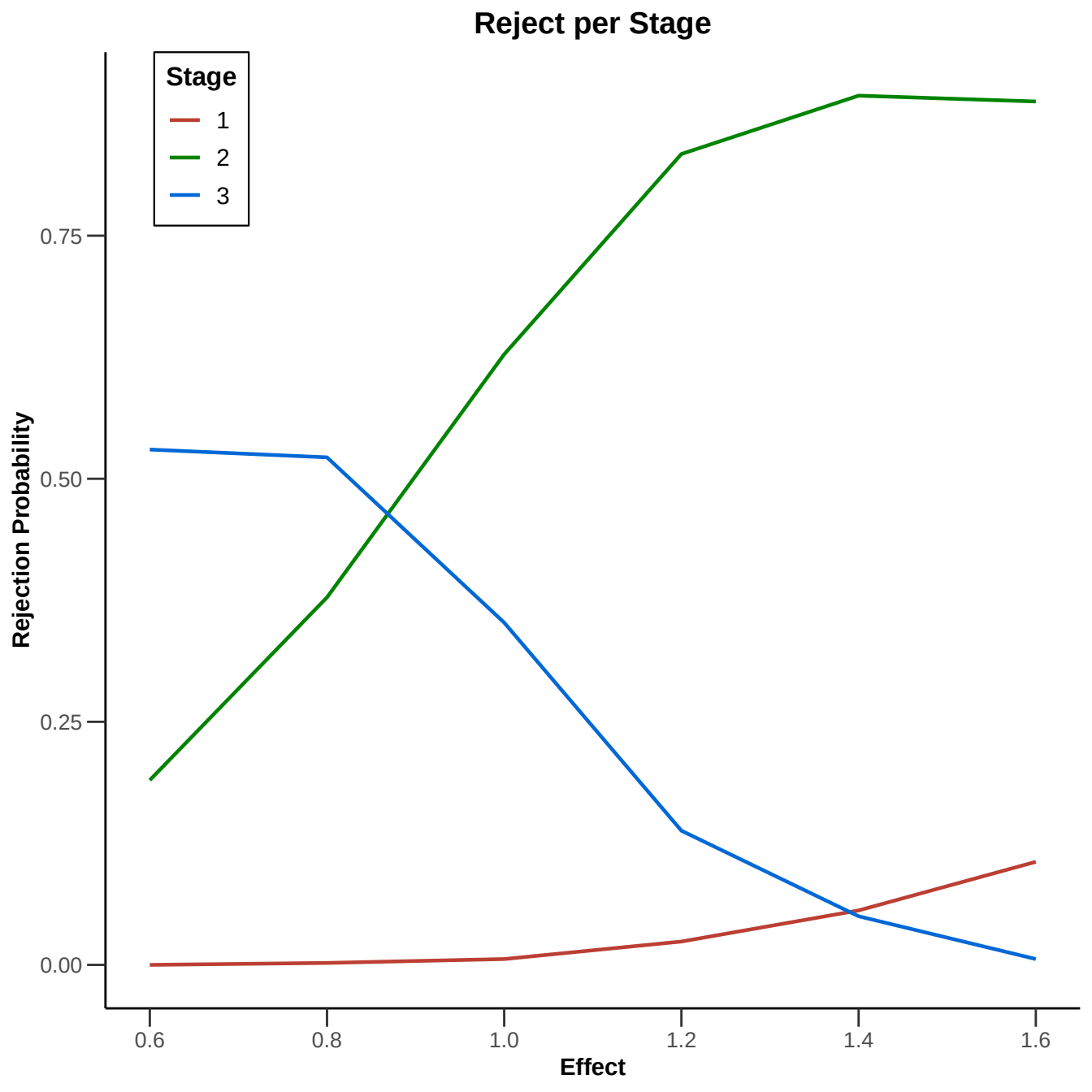
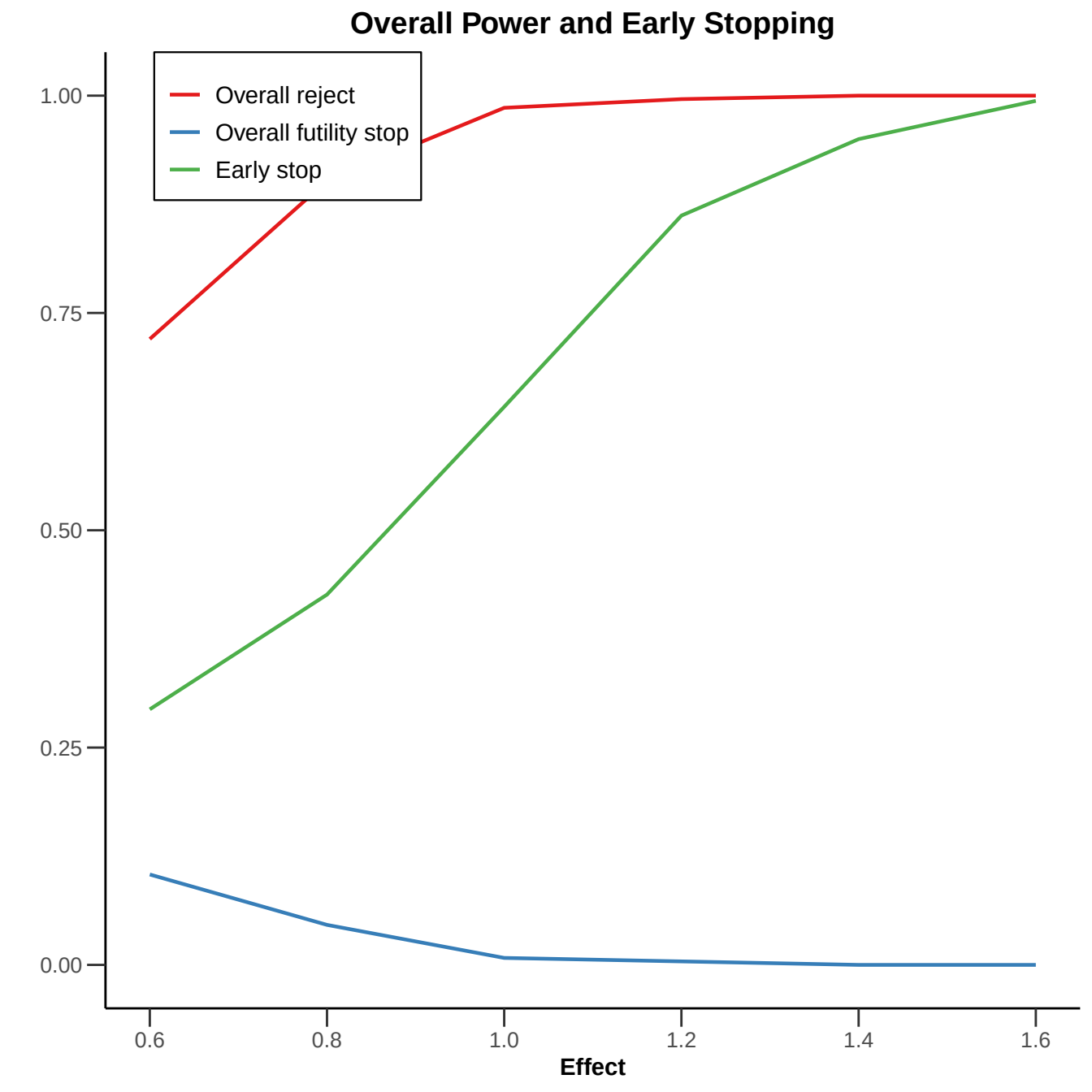
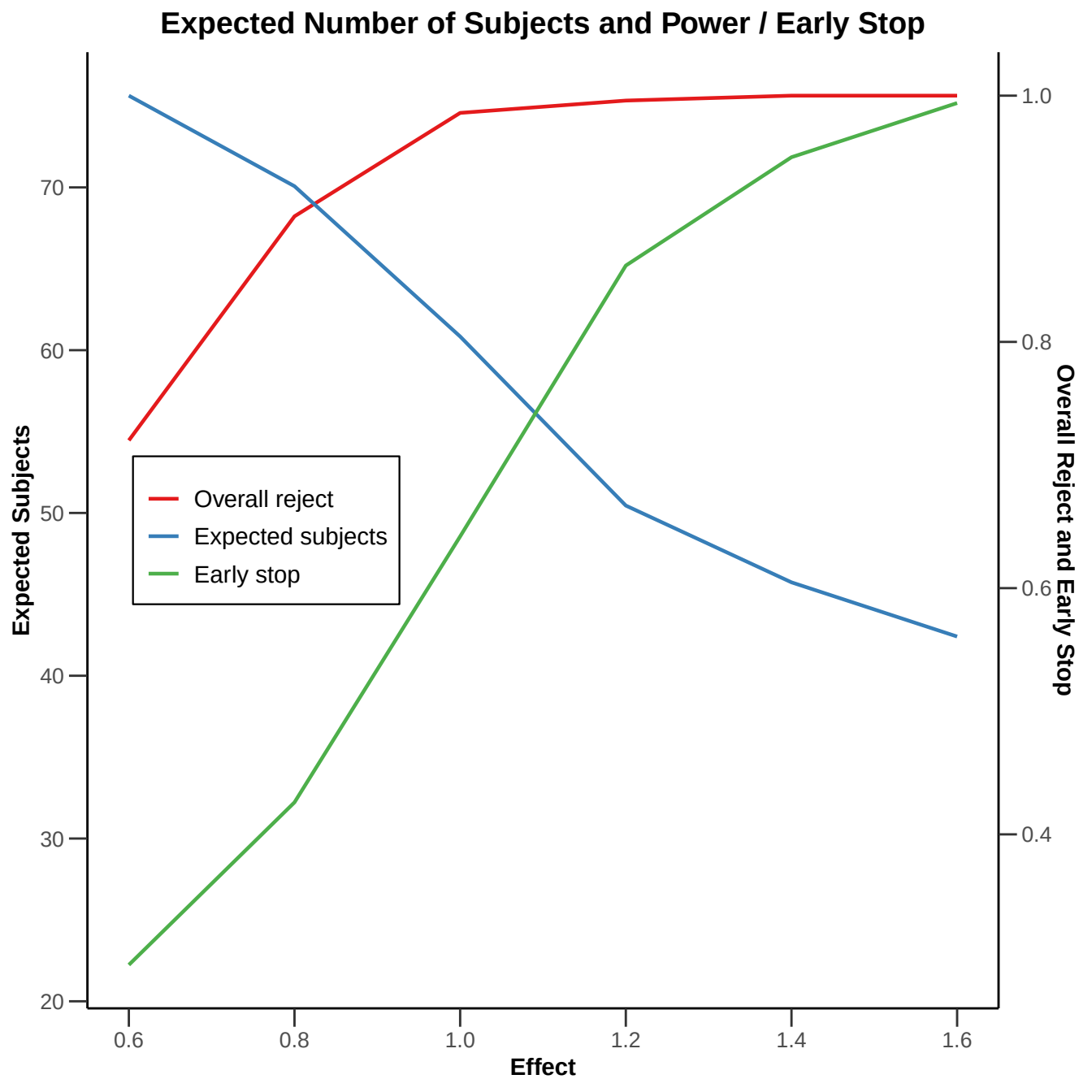
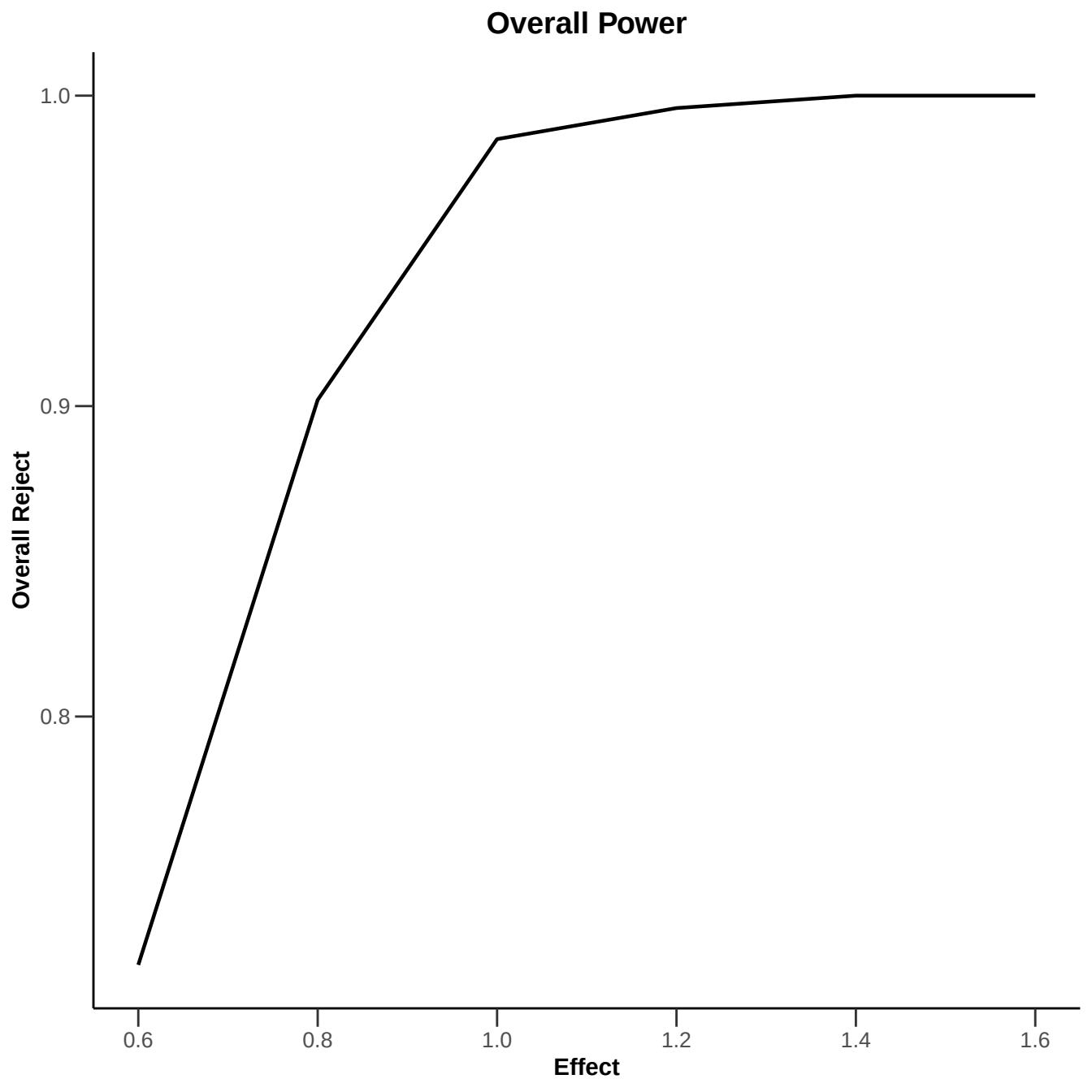
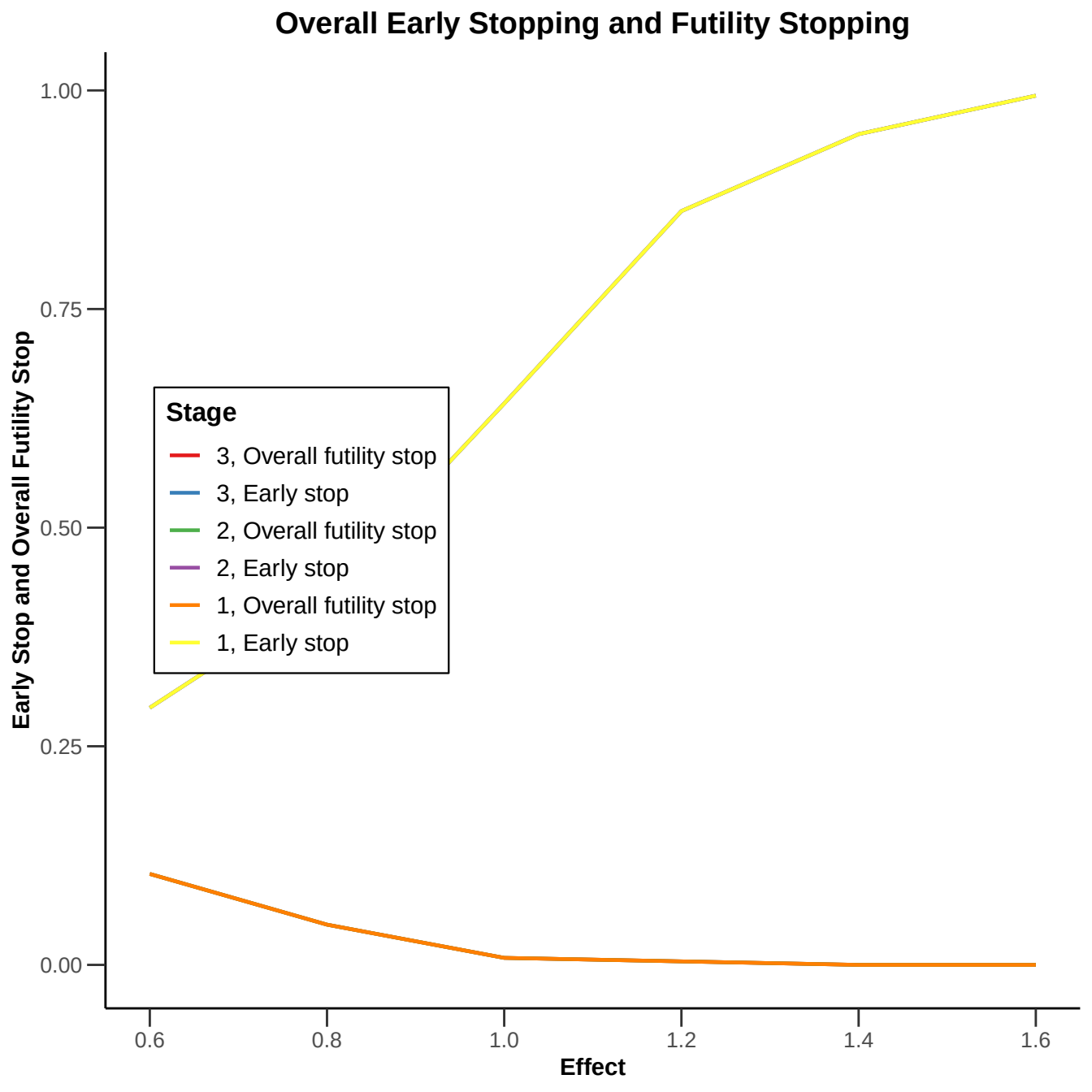
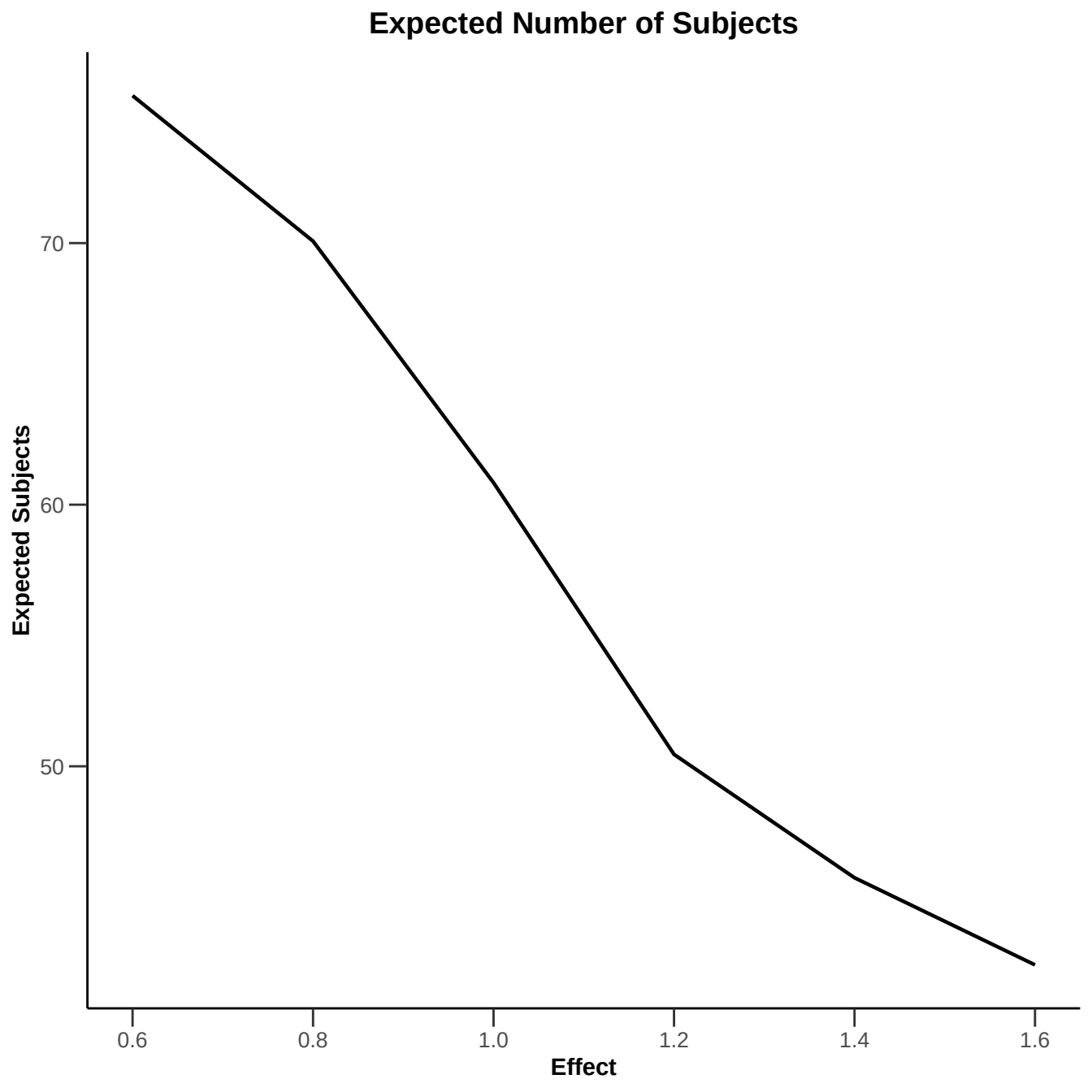

Reject per Stage
Stage
1
2
3
0.75
0.50
0.25
0.00
Rejection Probability
0.6
0.8
1.0
1.2
1.4
1.6
Effect

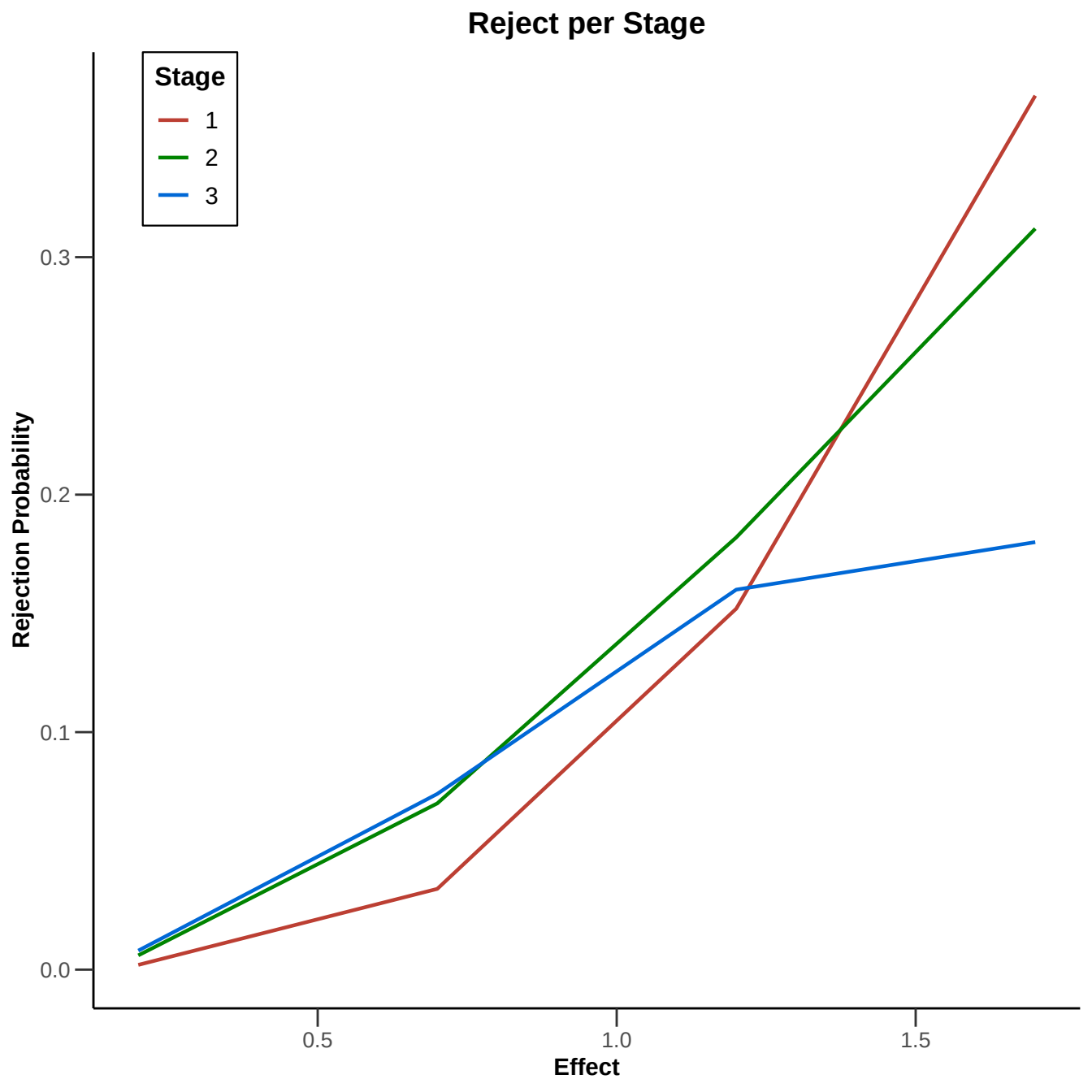

Overall Power and Early Stopping
Overall reject
Overall futility stop
Early stop
1.00
0.75
0.50
0.25
0.00
0.6
0.8
1.0
1.2
1.4
1.6
Effect

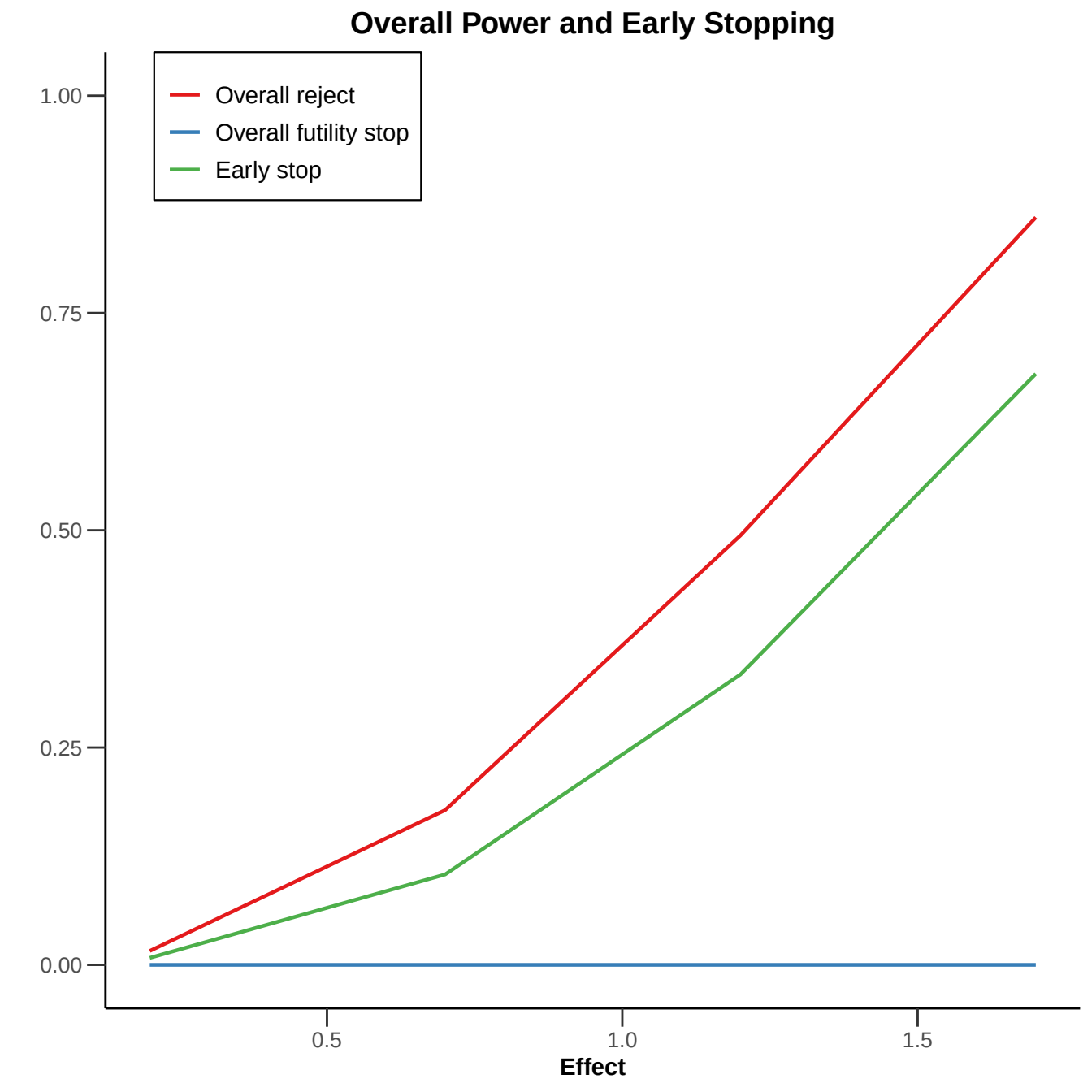

Expected Number of Subjects and Power / Early Stop
Expected Subjects
Overall Reject and Early Stop
Effect
Overall reject
Expected subjects
Early stop
20
30
40
50
60
70
0.4
0.6
0.8
1.0
0.6
0.8
1.0
1.2
1.4
1.6

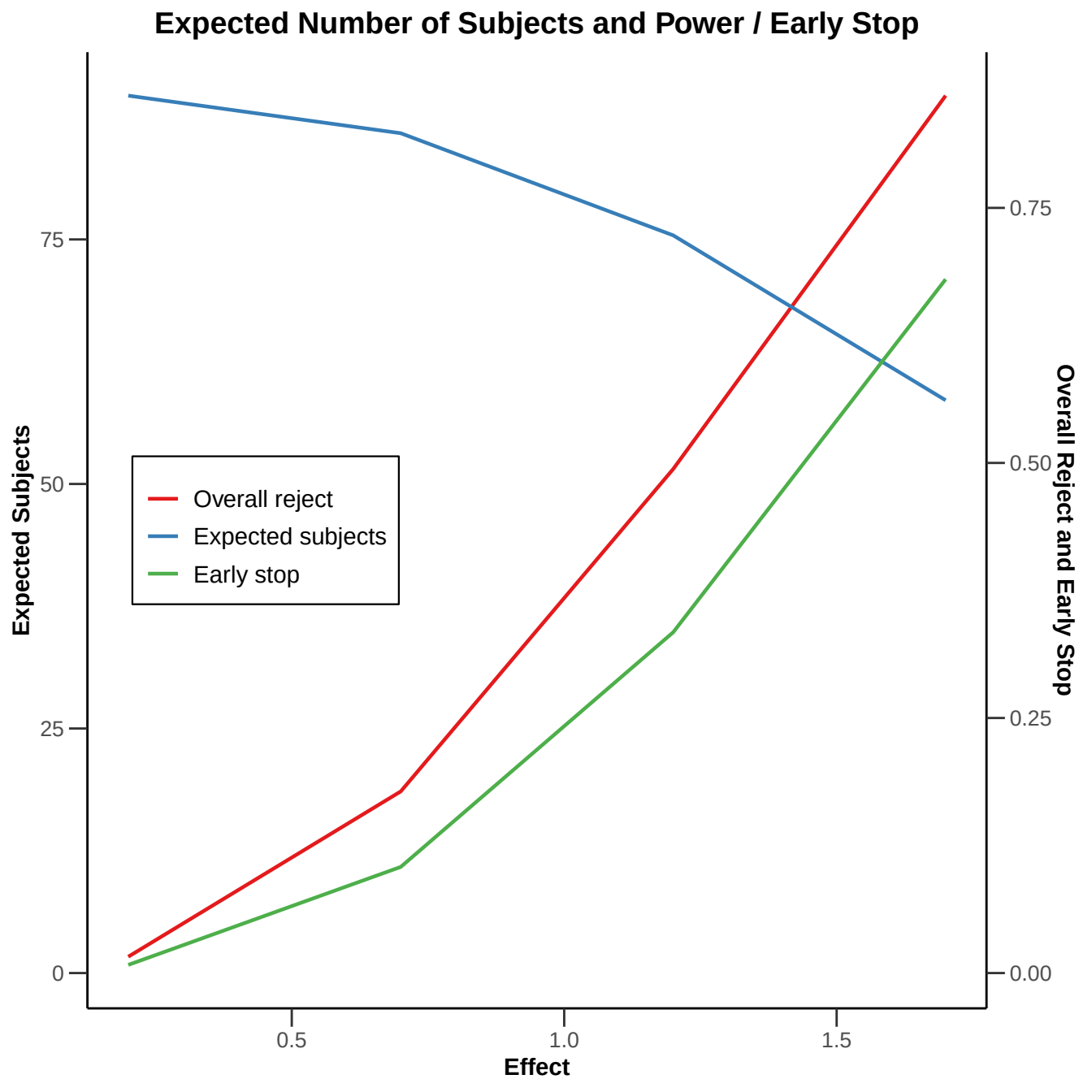

Overall Power
1.0
0.9
0.8
Overall Reject
0.6
0.8
1.0
1.2
1.4
1.6
Effect

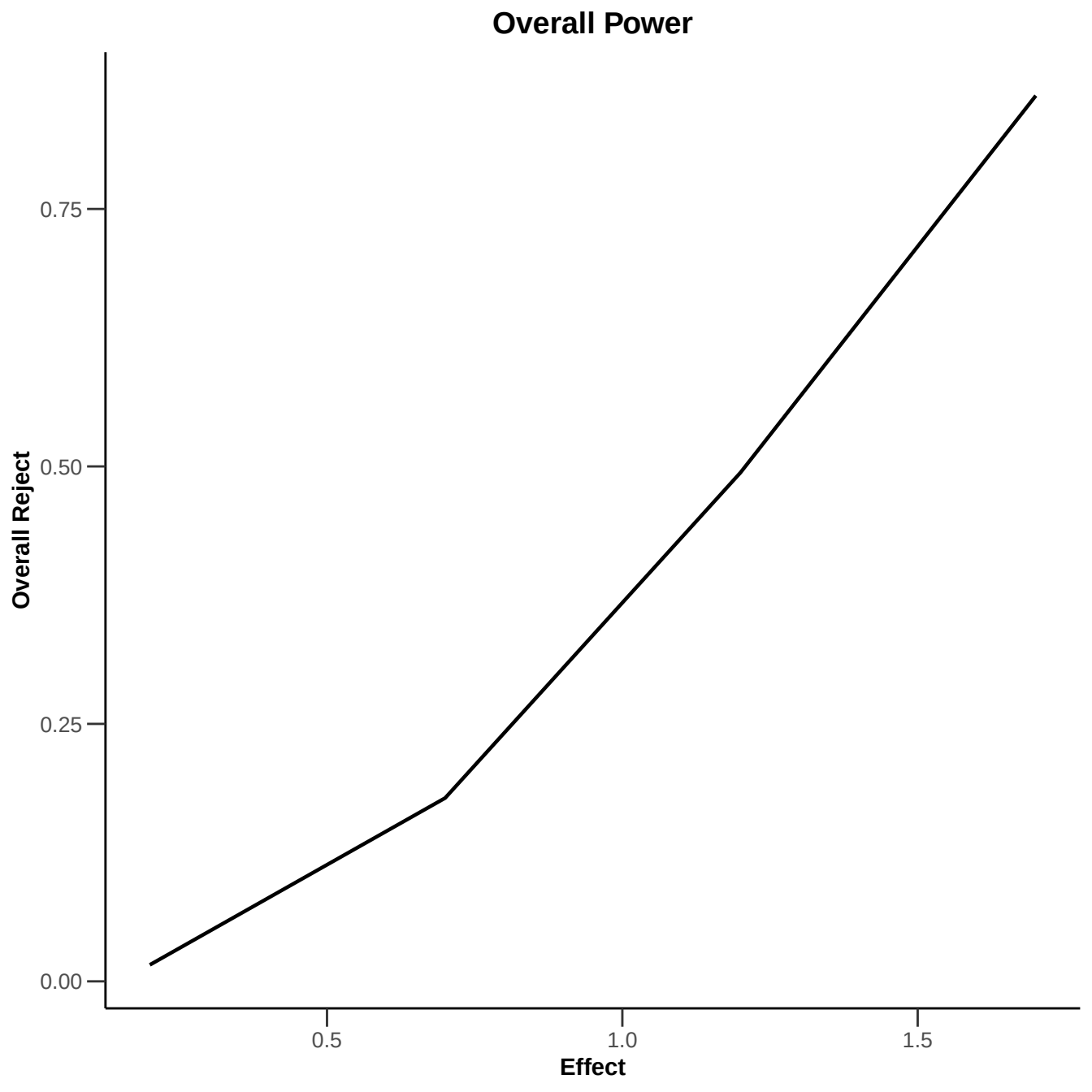

Overall Early Stopping and Futility Stopping
Early Stop and Overall Futility Stop
1.00
0.75
0.50
0.25
0.00
0.6
0.8
1.0
1.2
1.4
1.6
Effect
Stage
3, Overall futility stop
3, Early stop
2, Overall futility stop
2, Early stop
1, Overall futility stop
1, Early stop

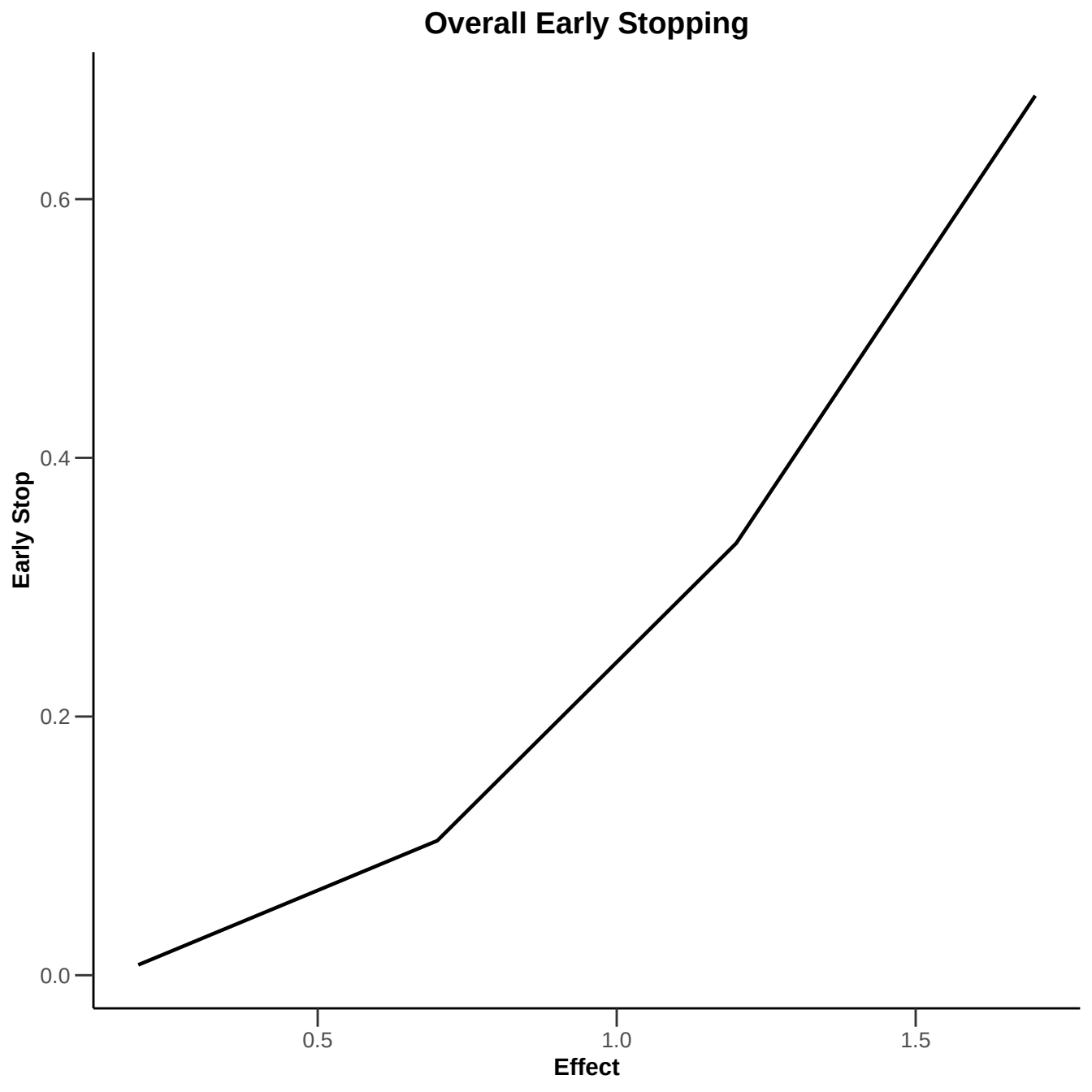

Expected Number of Subjects
Expected Subjects
70
60
50
0.6
0.8
1.0
1.2
1.4
1.6
Effect

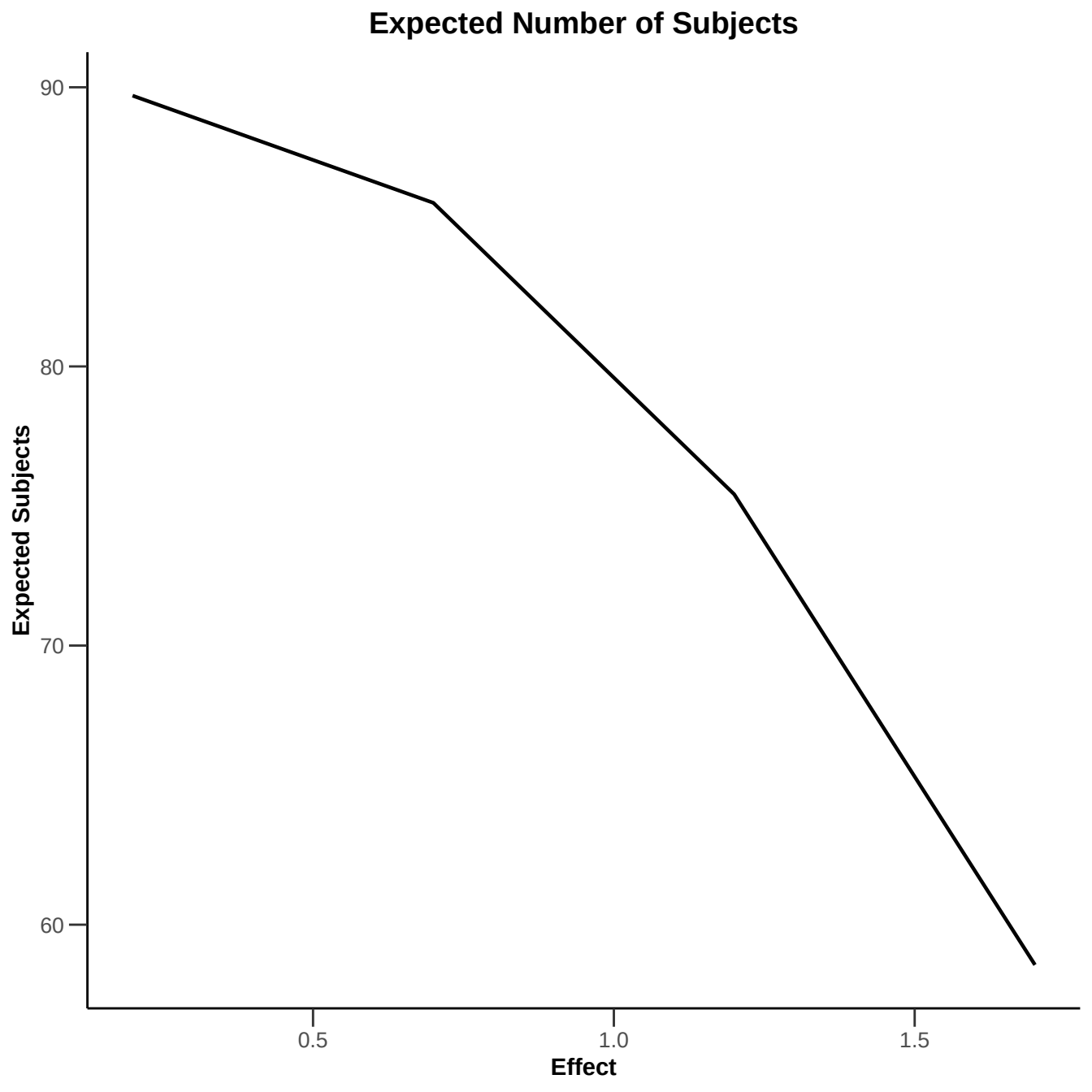

Reject per Stage
Stage
1
2
3
Rejection Probability
0.0
0.1
0.2
0.3
0.5
1.0
1.5
Effect

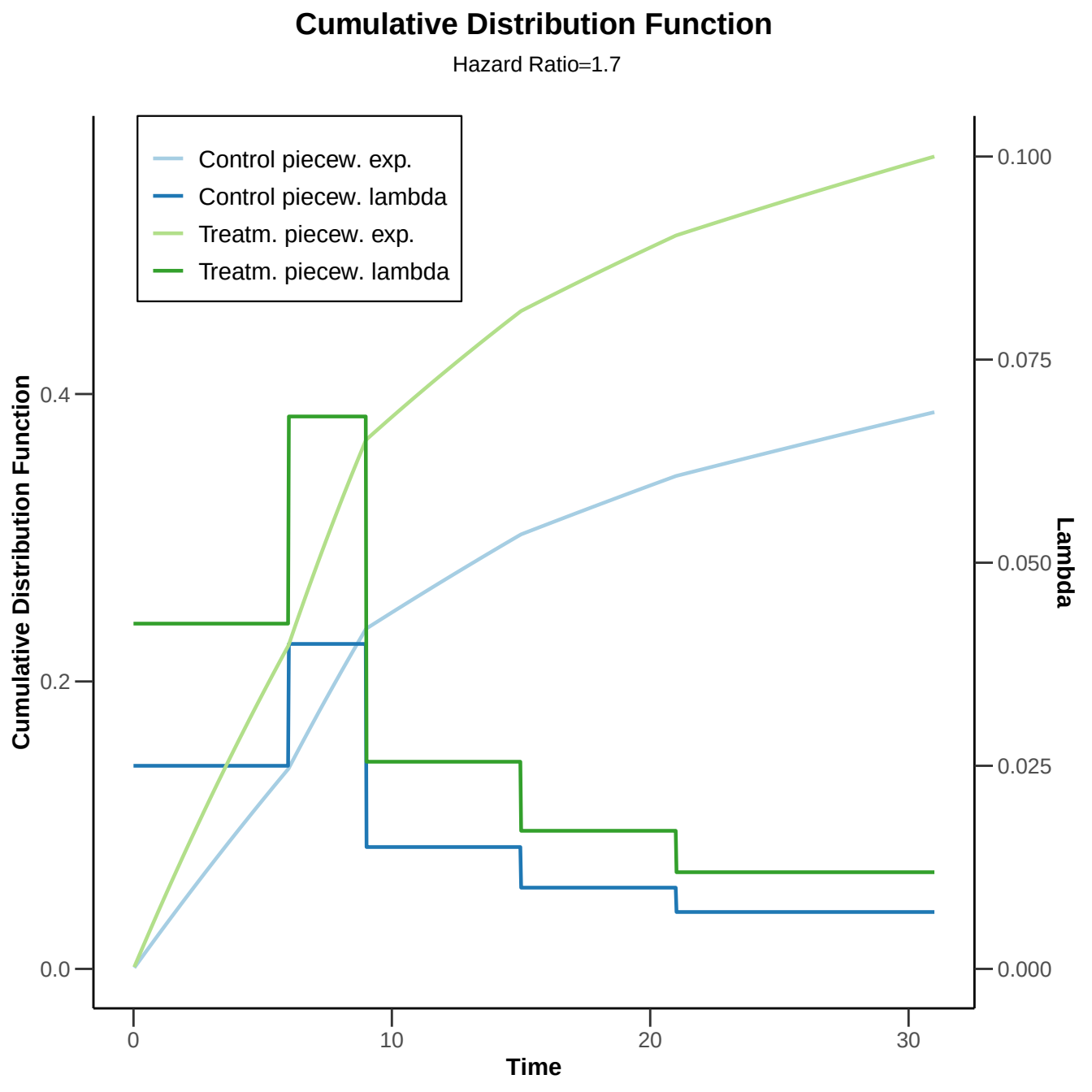

Overall Power and Early Stopping
Overall reject
Overall futility stop
Early stop
1.00
0.75
0.50
0.25
0.00
0.5
1.0
1.5
Effect

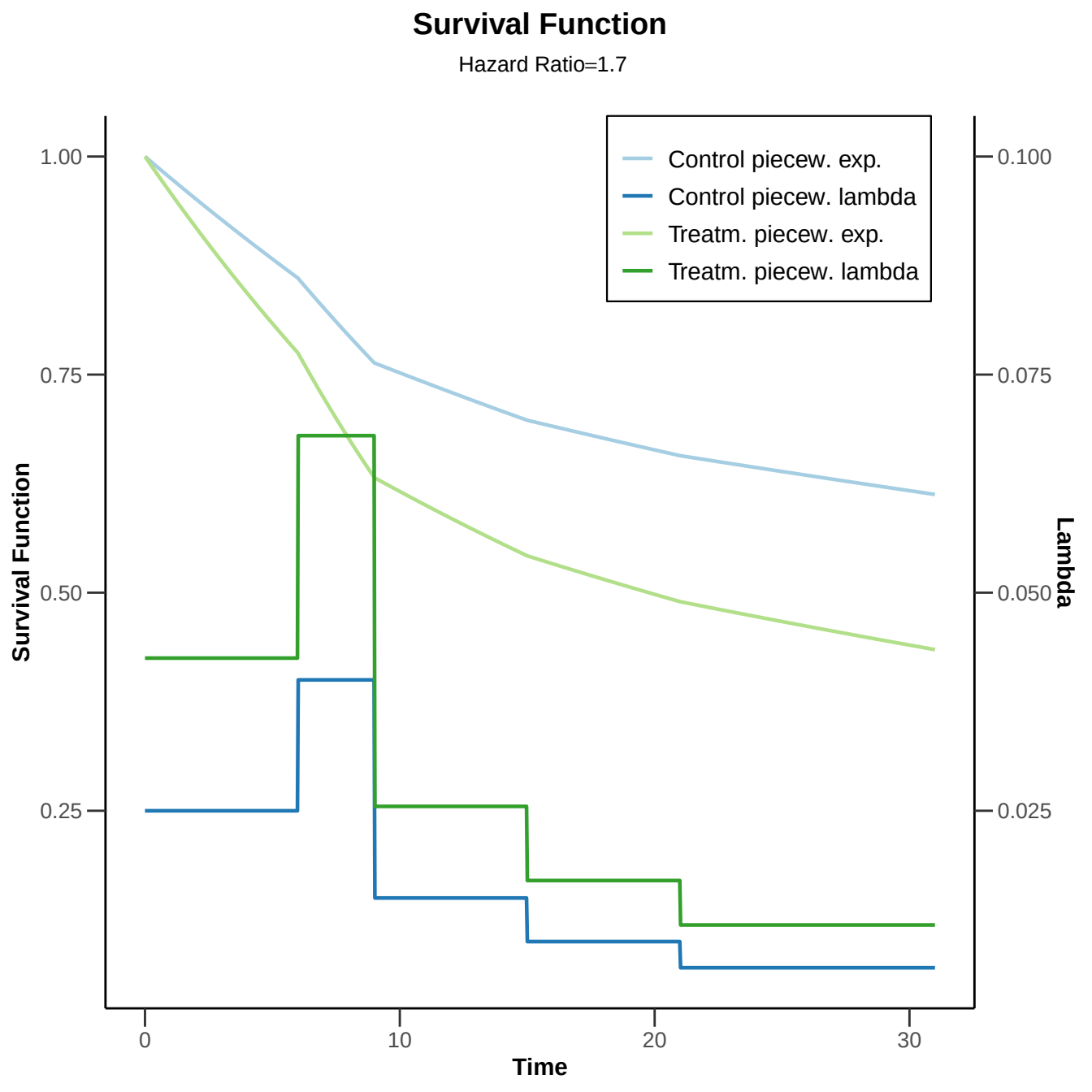

Expected Number of Subjects and Power / Early Stop
Expected Subjects
Overall Reject and Early Stop
Effect
Overall reject
Expected subjects
Early stop
0
25
50
75
0.00
0.25
0.50
0.75
0.5
1.0
1.5

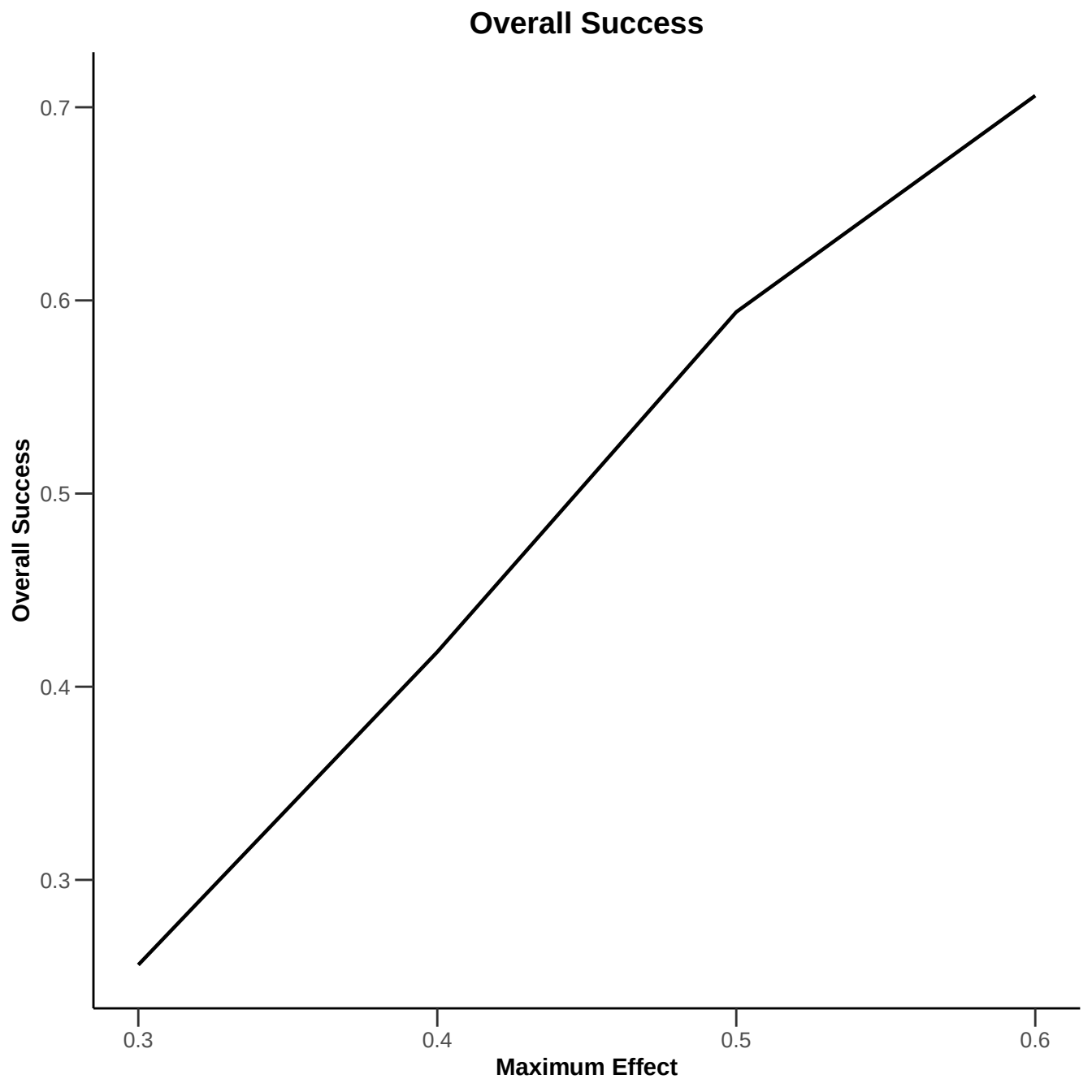

Overall Power
Overall Reject
0.75
0.50
0.25
0.00
0.5
1.0
1.5
Effect

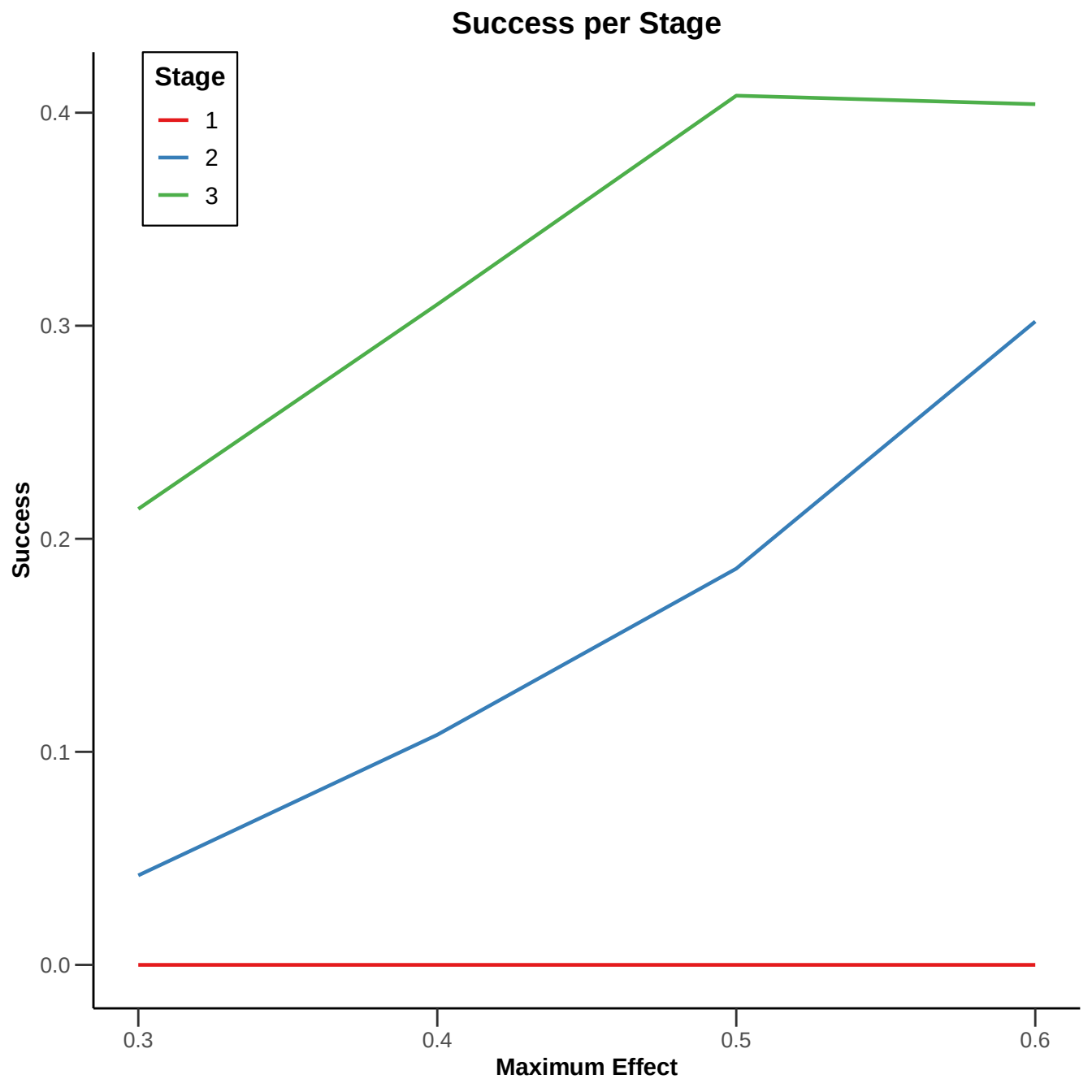

Overall Early Stopping
Early Stop
0.0
0.2
0.4
0.6
0.5
1.0
1.5
Effect

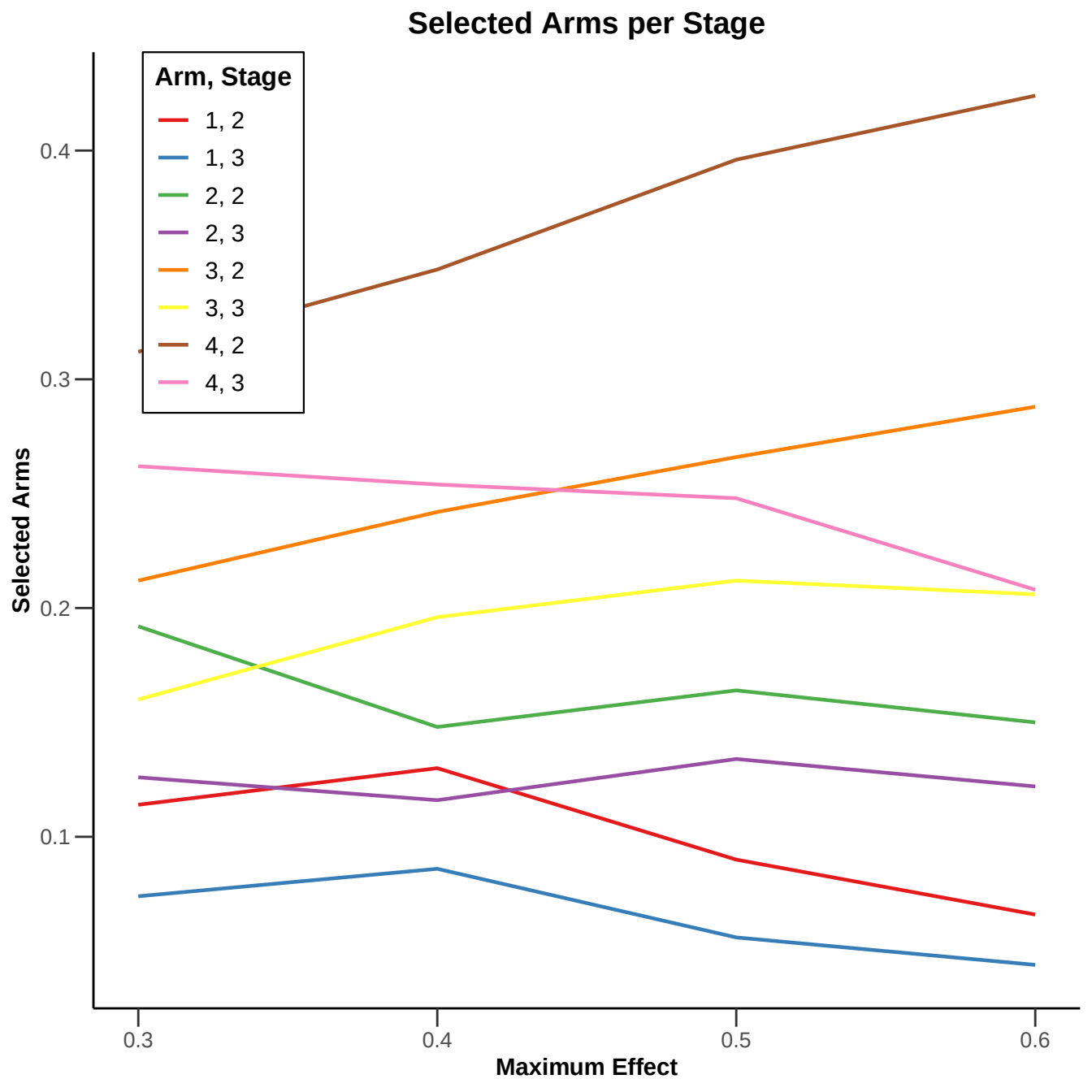

Expected Number of Subjects
90
80
70
60
Expected Subjects
0.5
1.0
1.5
Effect

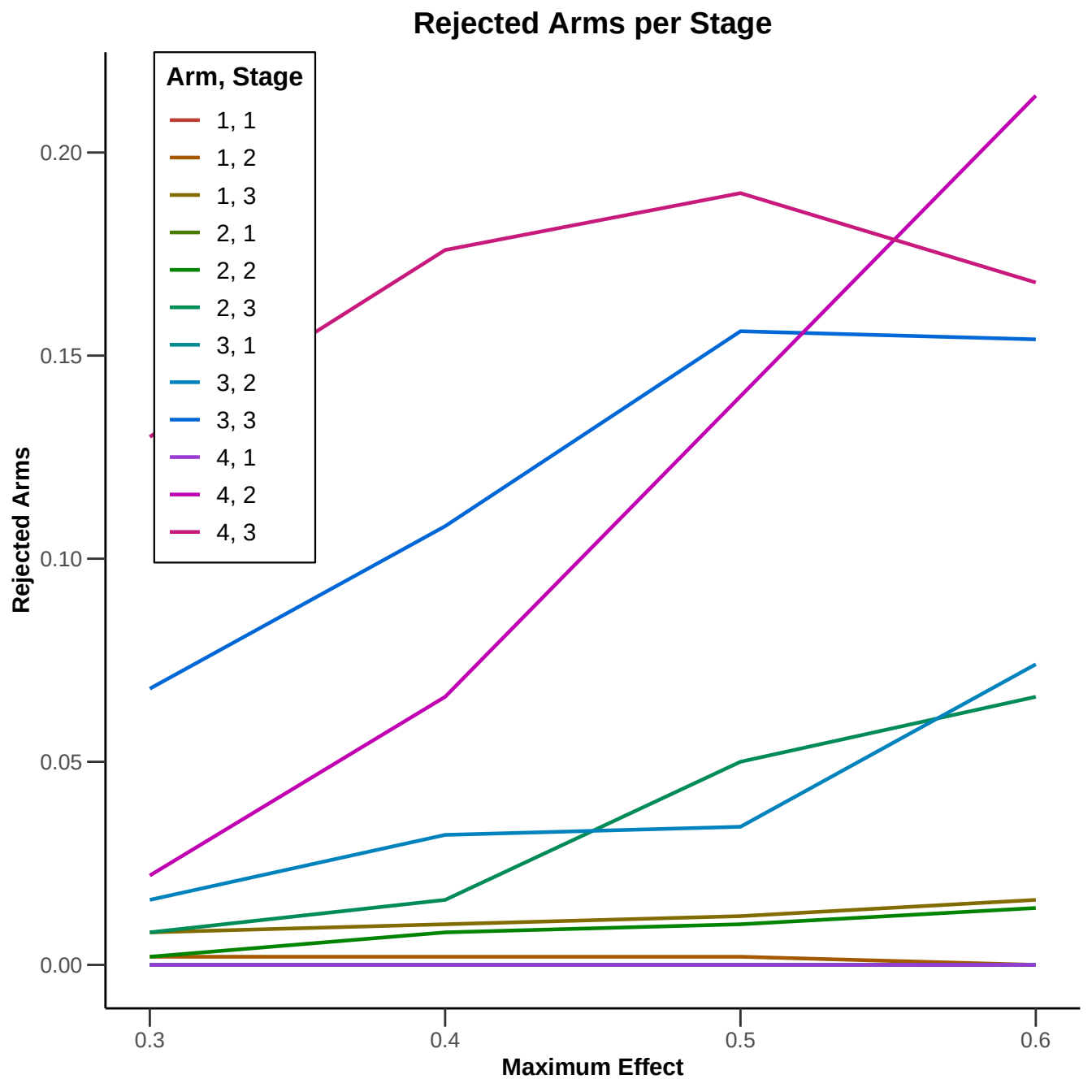

Cumulative Distribution Function
Hazard Ratio=1.7
Control piecew. exp.
Control piecew. lambda
Treatm. piecew. exp.
Treatm. piecew. lambda
Cumulative Distribution Function
0.0
0.2
0.4
Lambda
0.000
0.025
0.050
0.075
0.100
0
10
20
30
Time

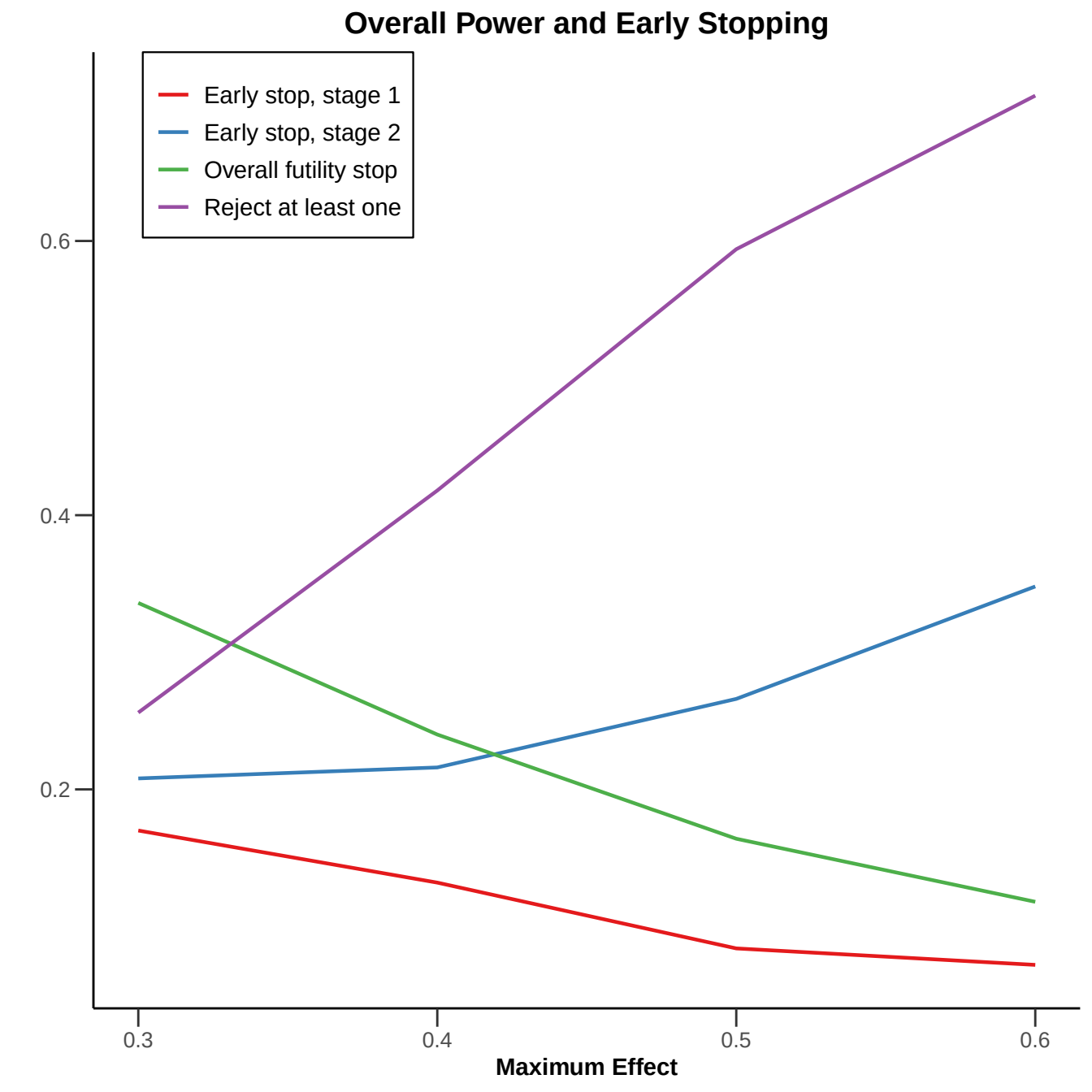

Survival Function
Hazard Ratio=1.7
Control piecew. exp.
Control piecew. lambda
Treatm. piecew. exp.
Treatm. piecew. lambda
1.00
0.75
0.50
0.25
0.100
0.075
0.050
0.025
Survival Function
Lambda
0
10
20
30
Time

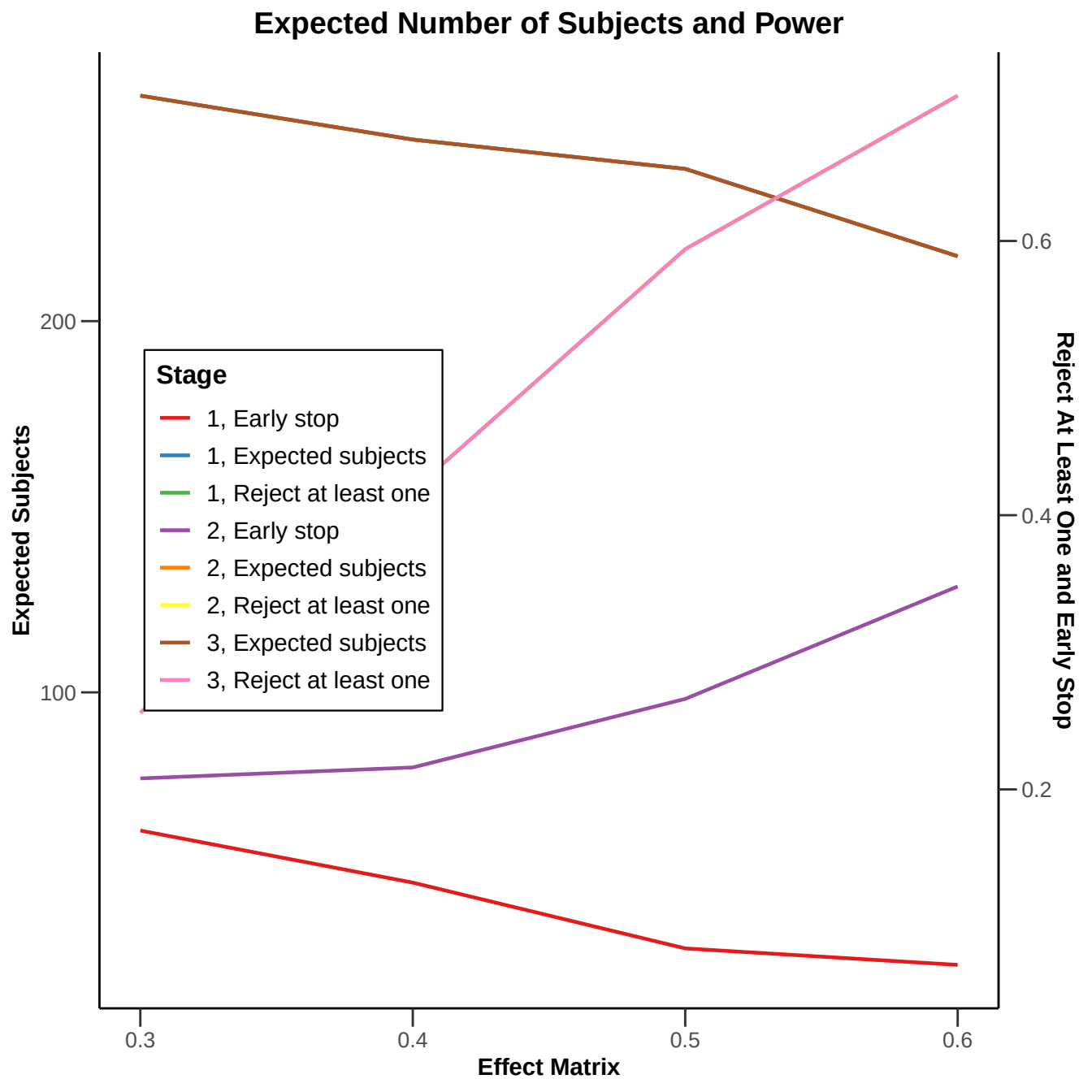

Overall Success
0.7
0.6
0.5
0.4
0.3
Overall Success
0.3
0.4
0.5
0.6
Maximum Effect

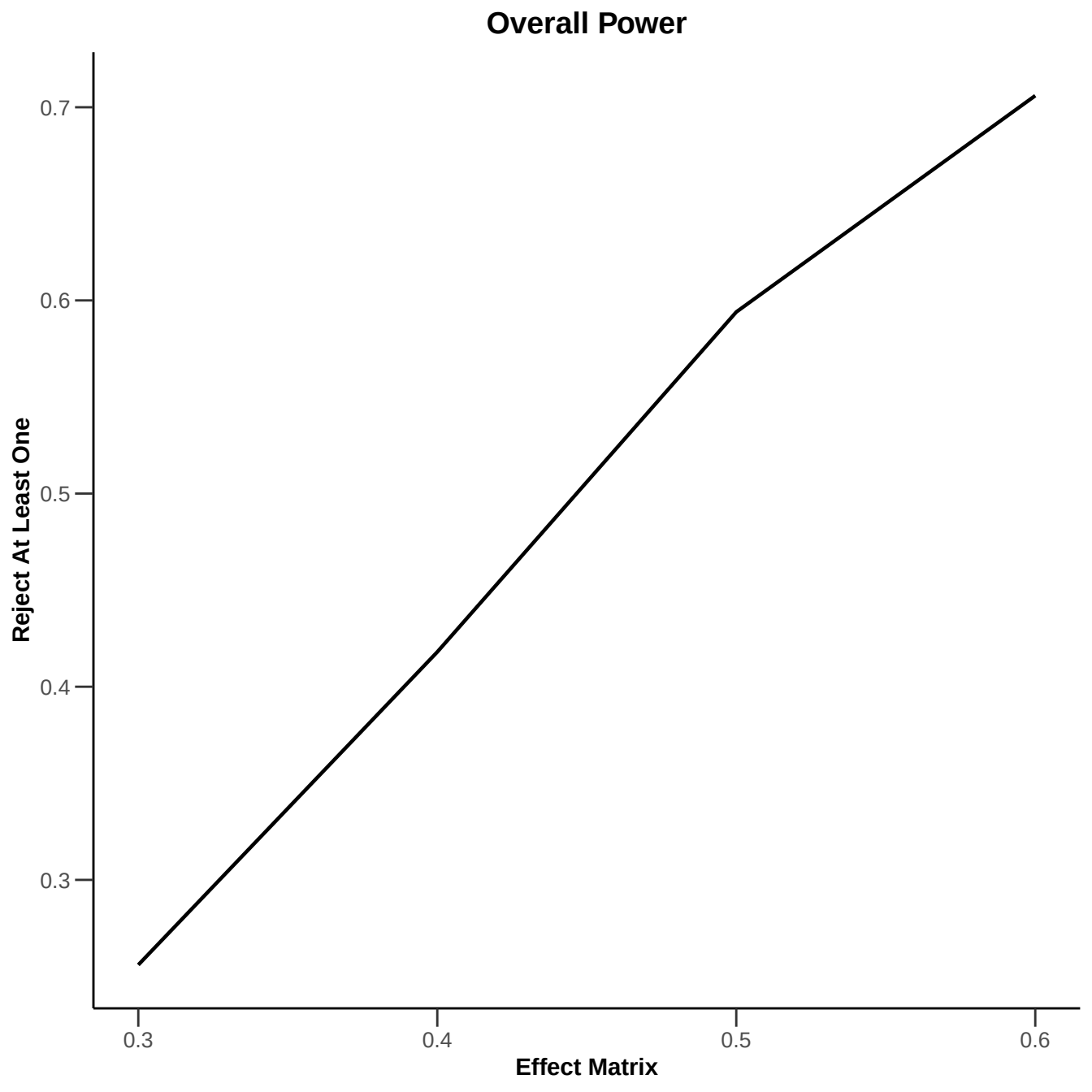

Success per Stage
Stage
1
2
3
0.4
0.3
0.2
0.1
0.0
Success
0.3
0.4
0.5
0.6
Maximum Effect

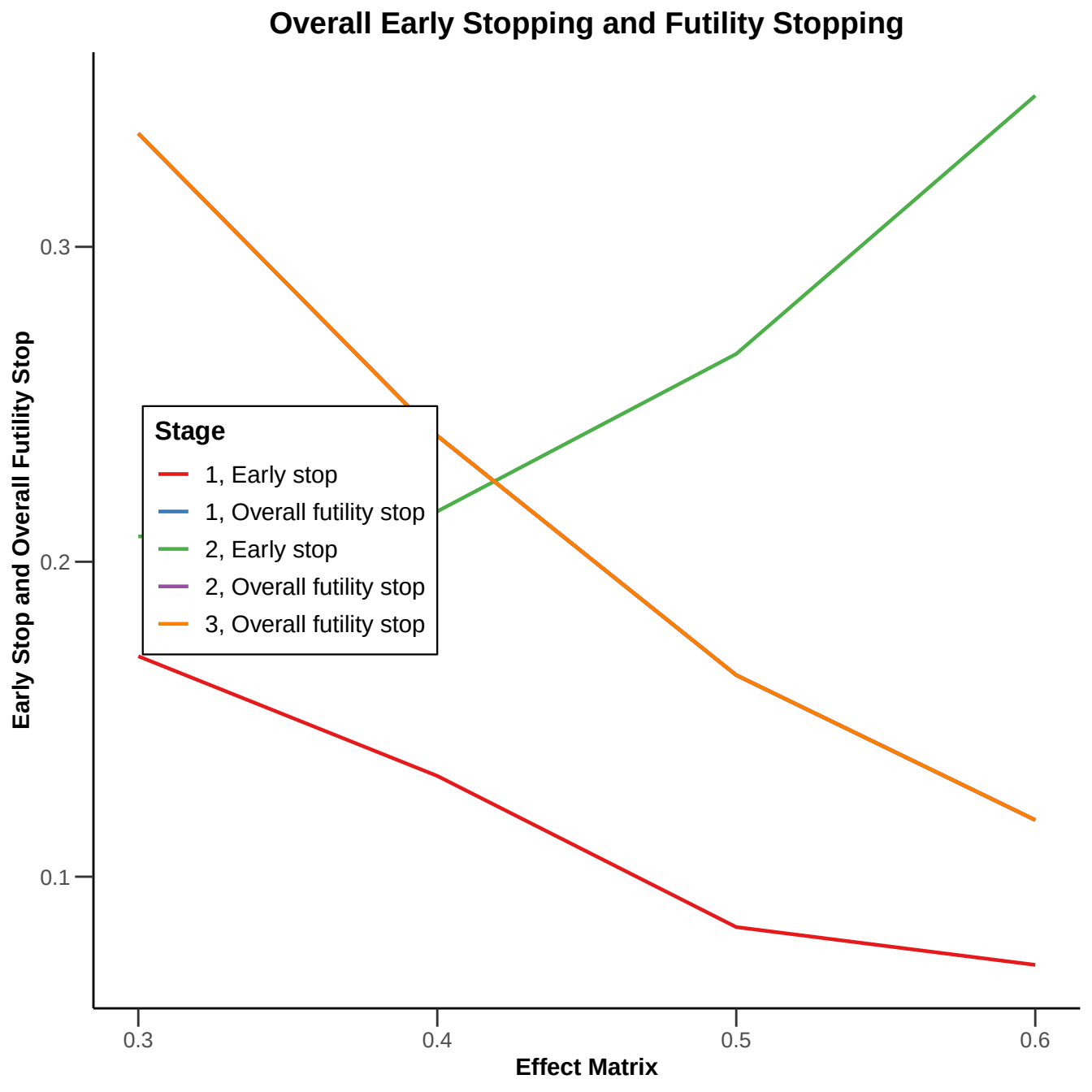

Selected Arms per Stage
Arm, Stage
1, 2
1, 3
2, 2
2, 3
3, 2
3, 3
4, 2
4, 3
Selected Arms
0.4
0.3
0.2
0.1
0.3
0.4
0.5
0.6
Maximum Effect

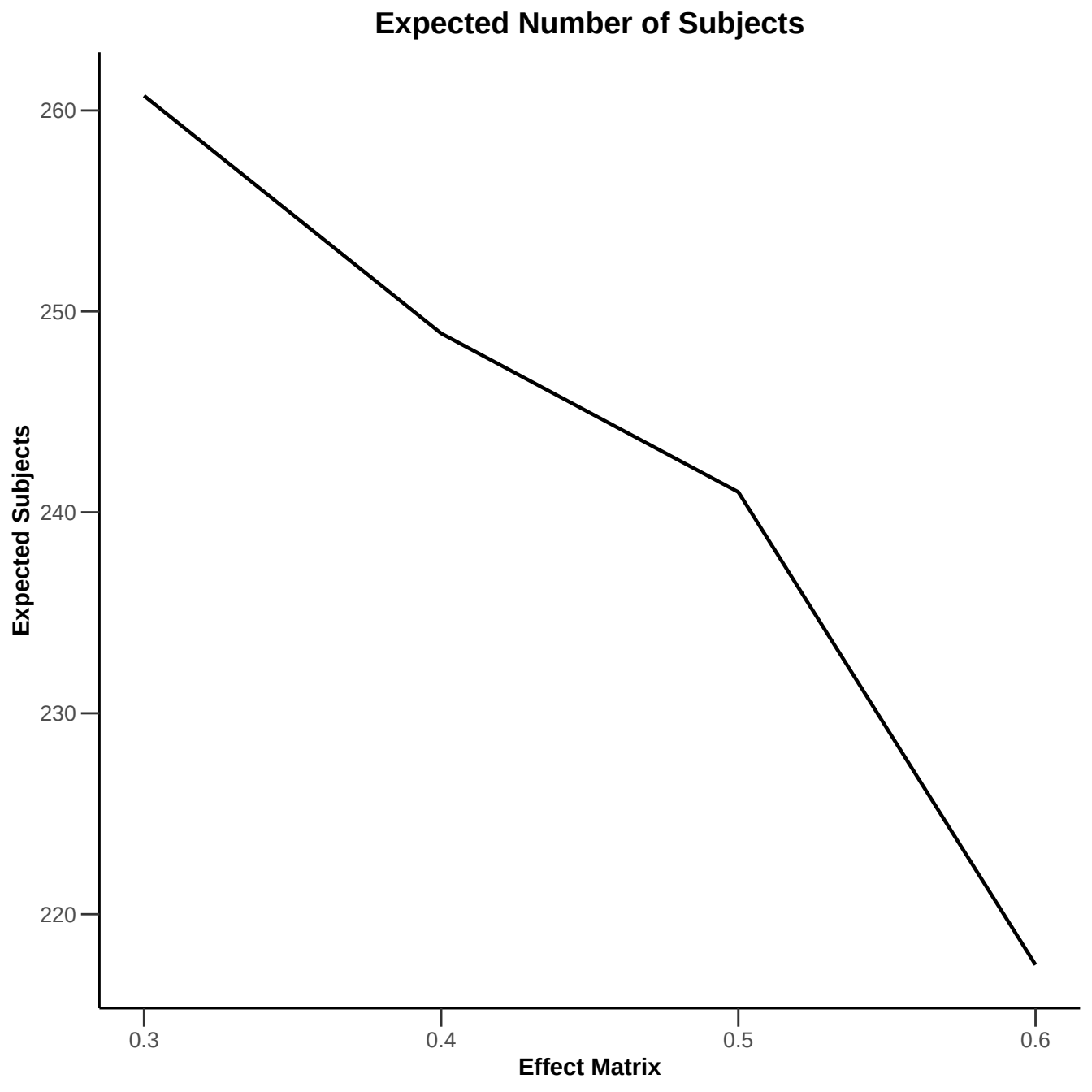

Rejected Arms per Stage
Arm, Stage
1, 1
1, 2
1, 3
2, 1
2, 2
2, 3
3, 1
3, 2
3, 3
4, 1
4, 2
4, 3
0.20
0.15
0.10
0.05
0.00
Rejected Arms
0.3
0.4
0.5
0.6
Maximum Effect

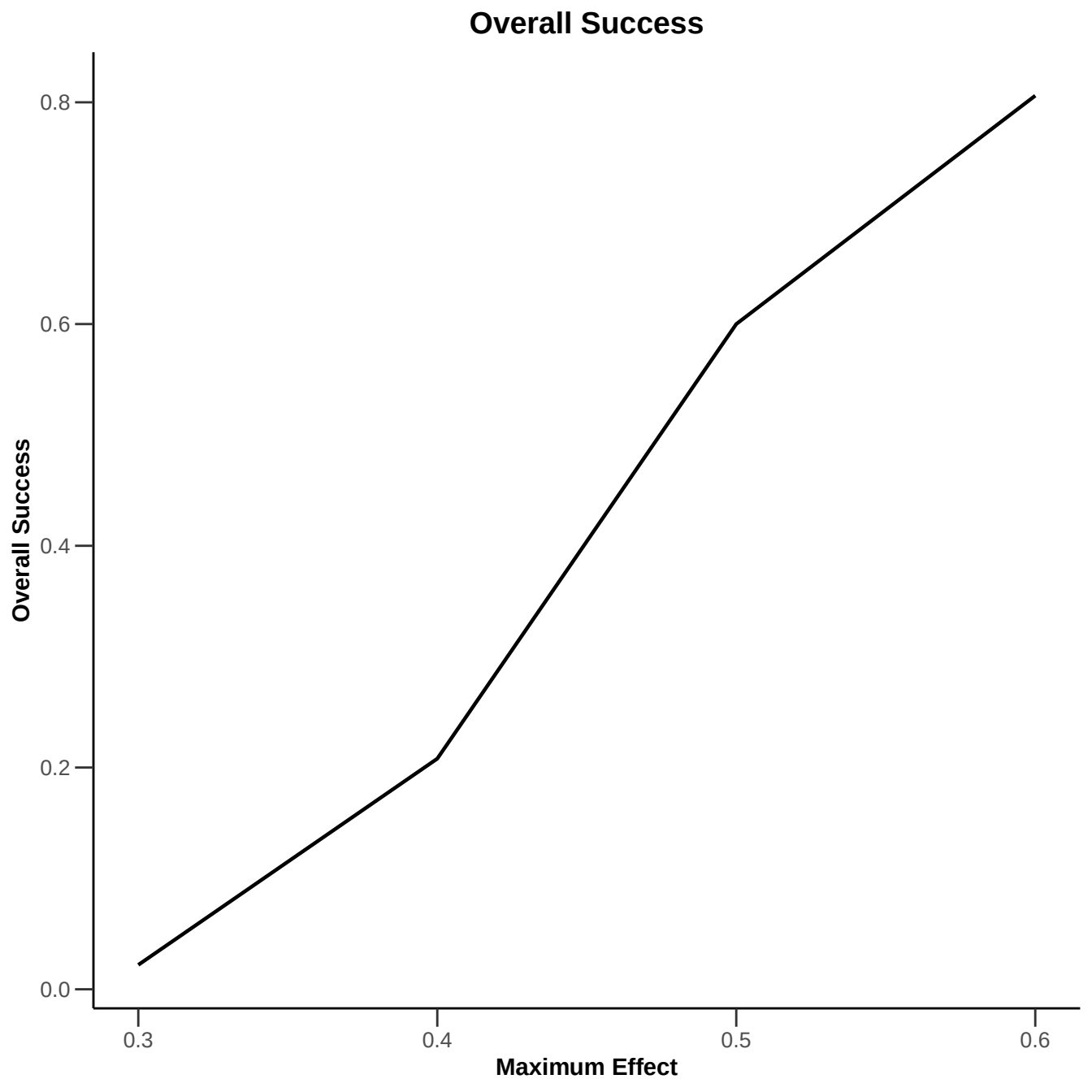

Overall Power and Early Stopping
Early stop, stage 1
Early stop, stage 2
Overall futility stop
Reject at least one
0.6
0.4
0.2
0.3
0.4
0.5
0.6
Maximum Effect

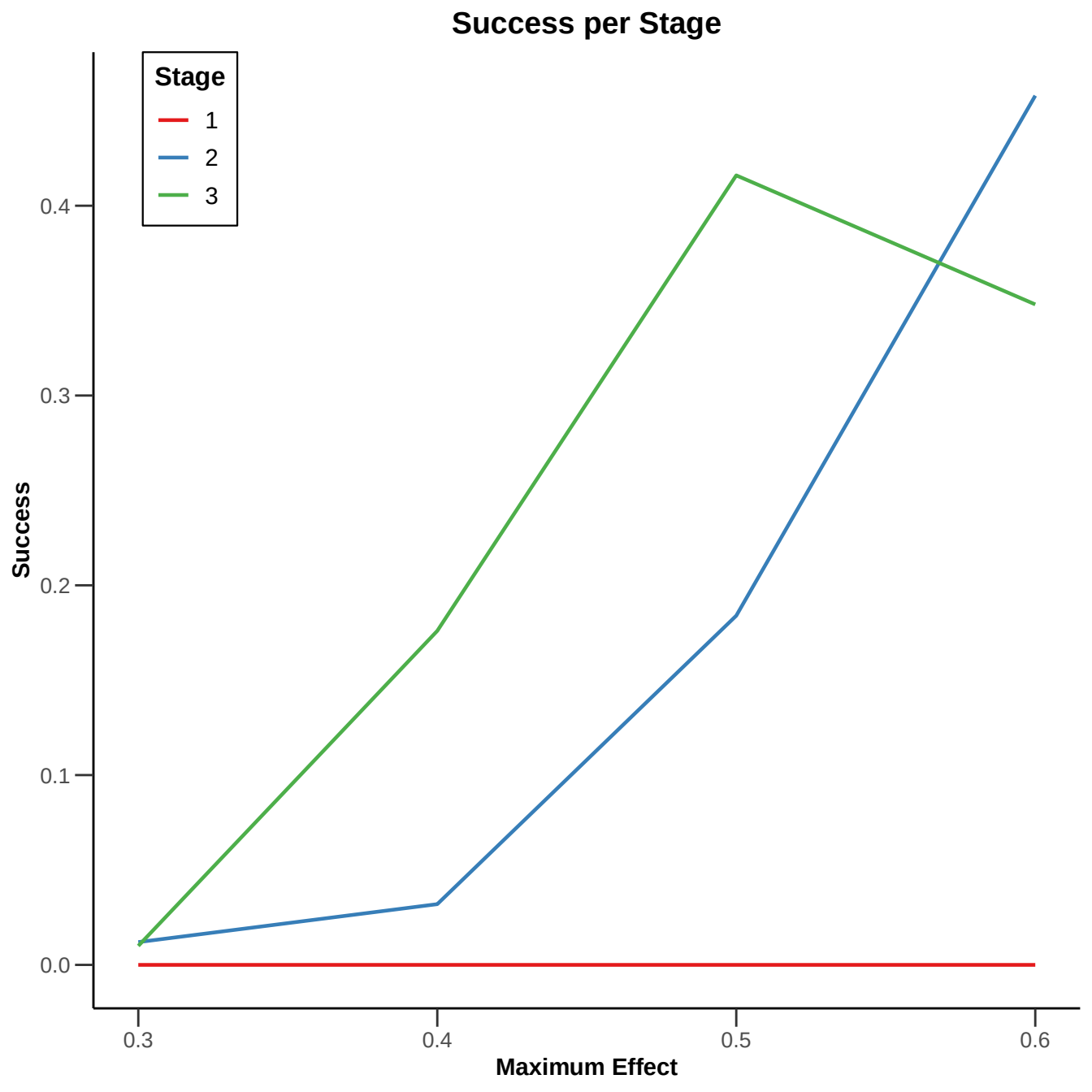

Expected Number of Subjects and Power
Expected Subjects
200
100
Reject At Least One and Early Stop
0.6
0.4
0.2
Stage
1, Early stop
1, Expected subjects
1, Reject at least one
2, Early stop
2, Expected subjects
2, Reject at least one
3, Expected subjects
3, Reject at least one
0.3
0.4
0.5
0.6
Effect Matrix

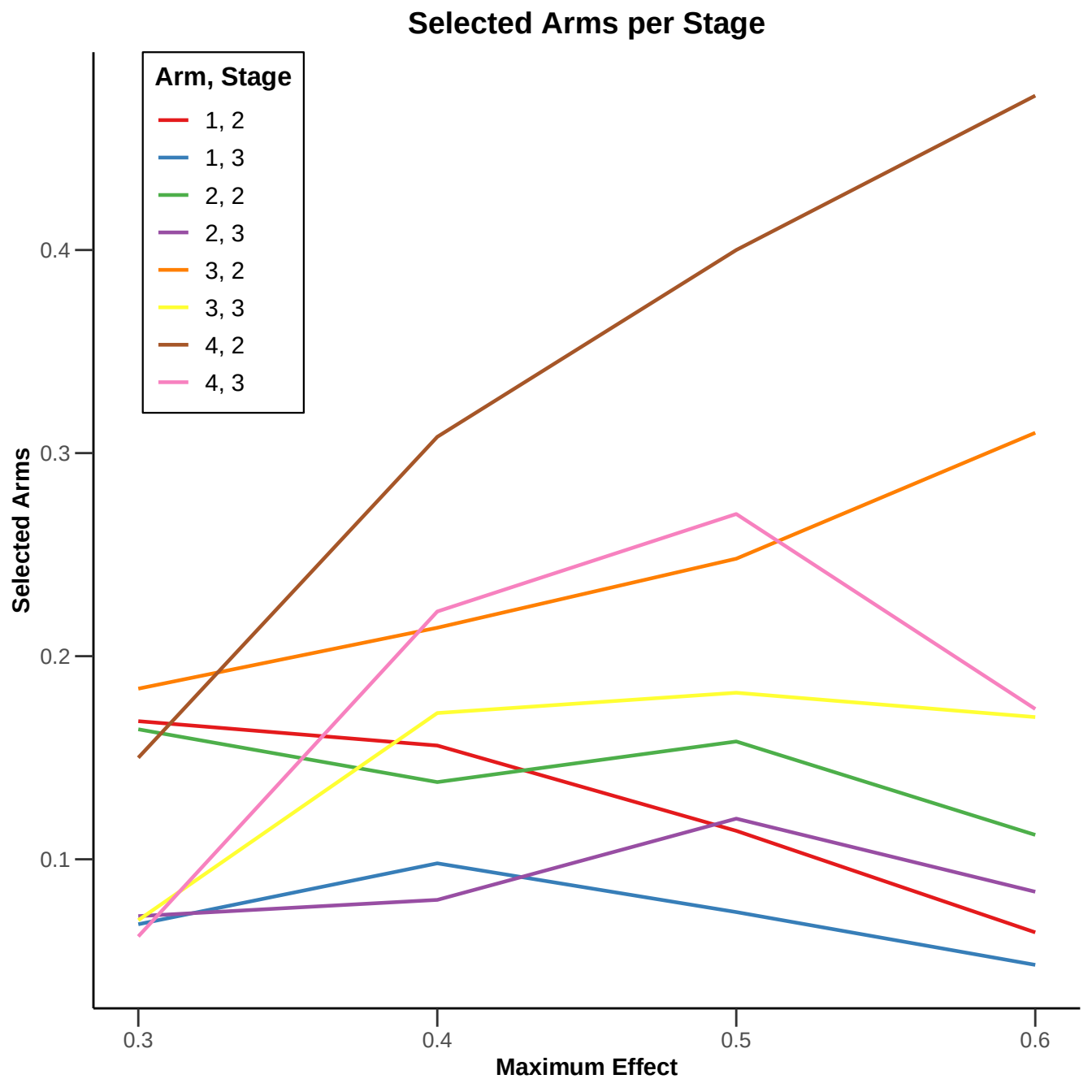

Overall Power
Reject At Least One
0.7
0.6
0.5
0.4
0.3
0.3
0.4
0.5
0.6
Effect Matrix

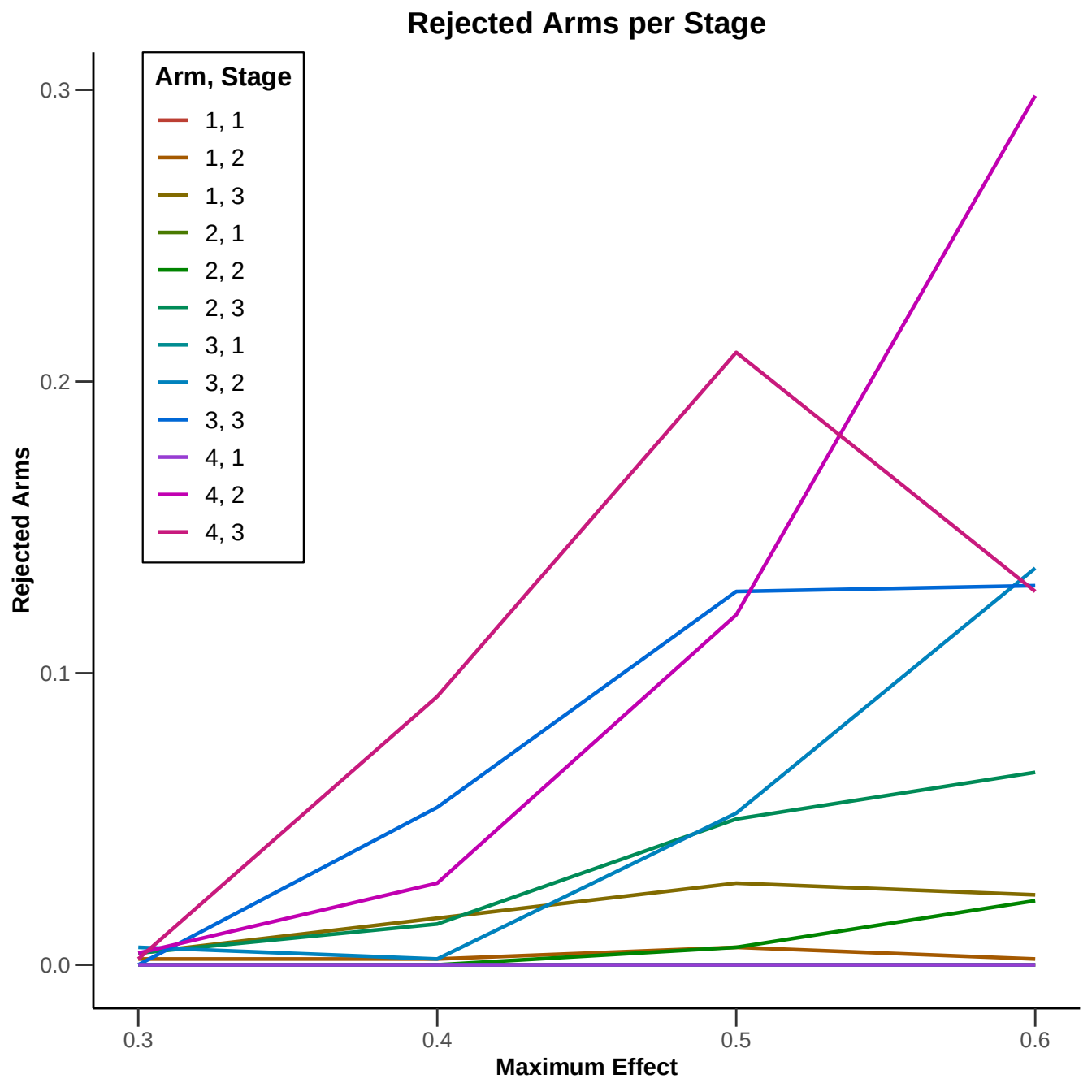

Overall Early Stopping and Futility Stopping
Early Stop and Overall Futility Stop
0.3
0.2
0.1
Stage
1, Early stop
1, Overall futility stop
2, Early stop
2, Overall futility stop
3, Overall futility stop
0.3
0.4
0.5
0.6
Effect Matrix

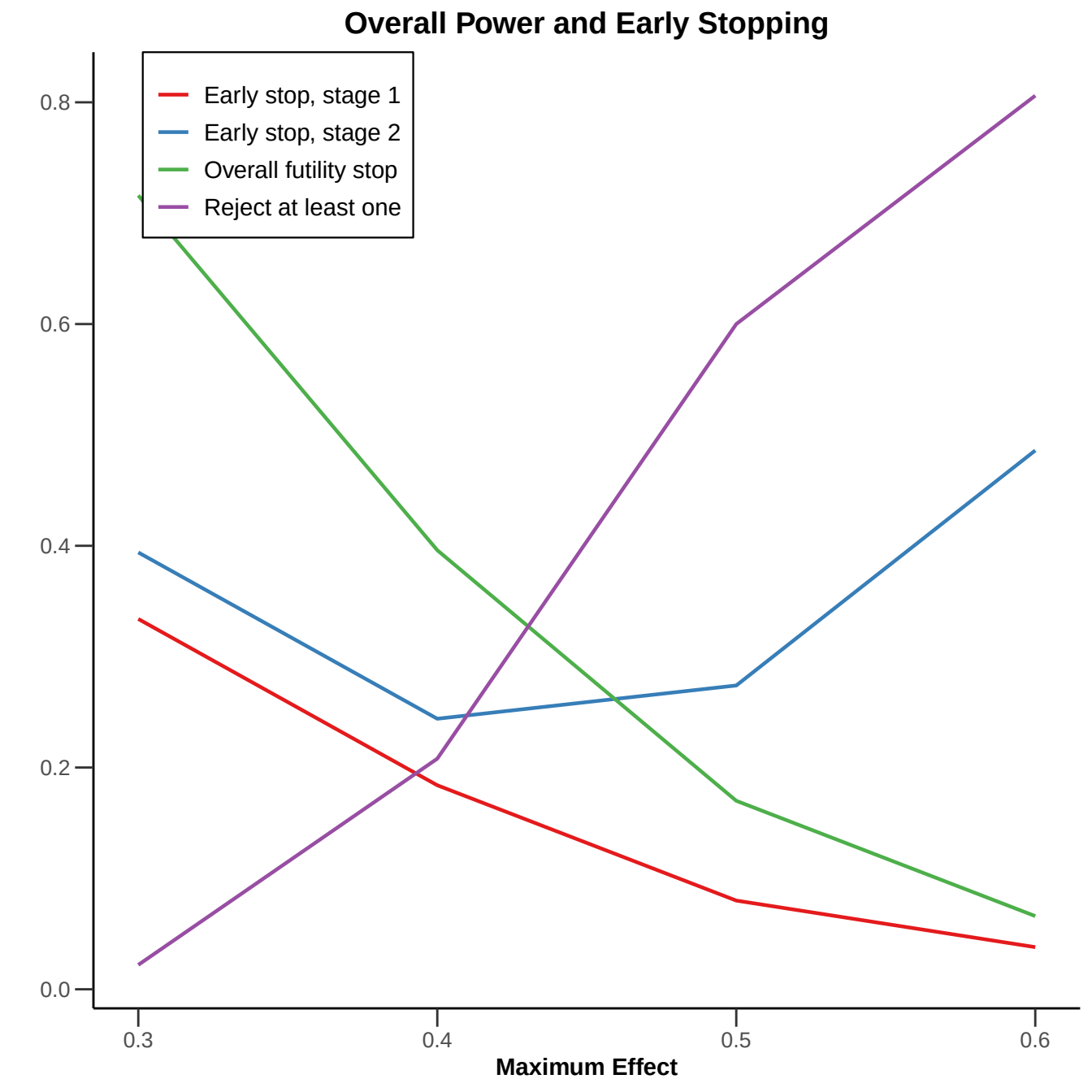

Expected Number of Subjects
260
250
240
230
220
Expected Subjects
0.3
0.4
0.5
0.6
Effect Matrix

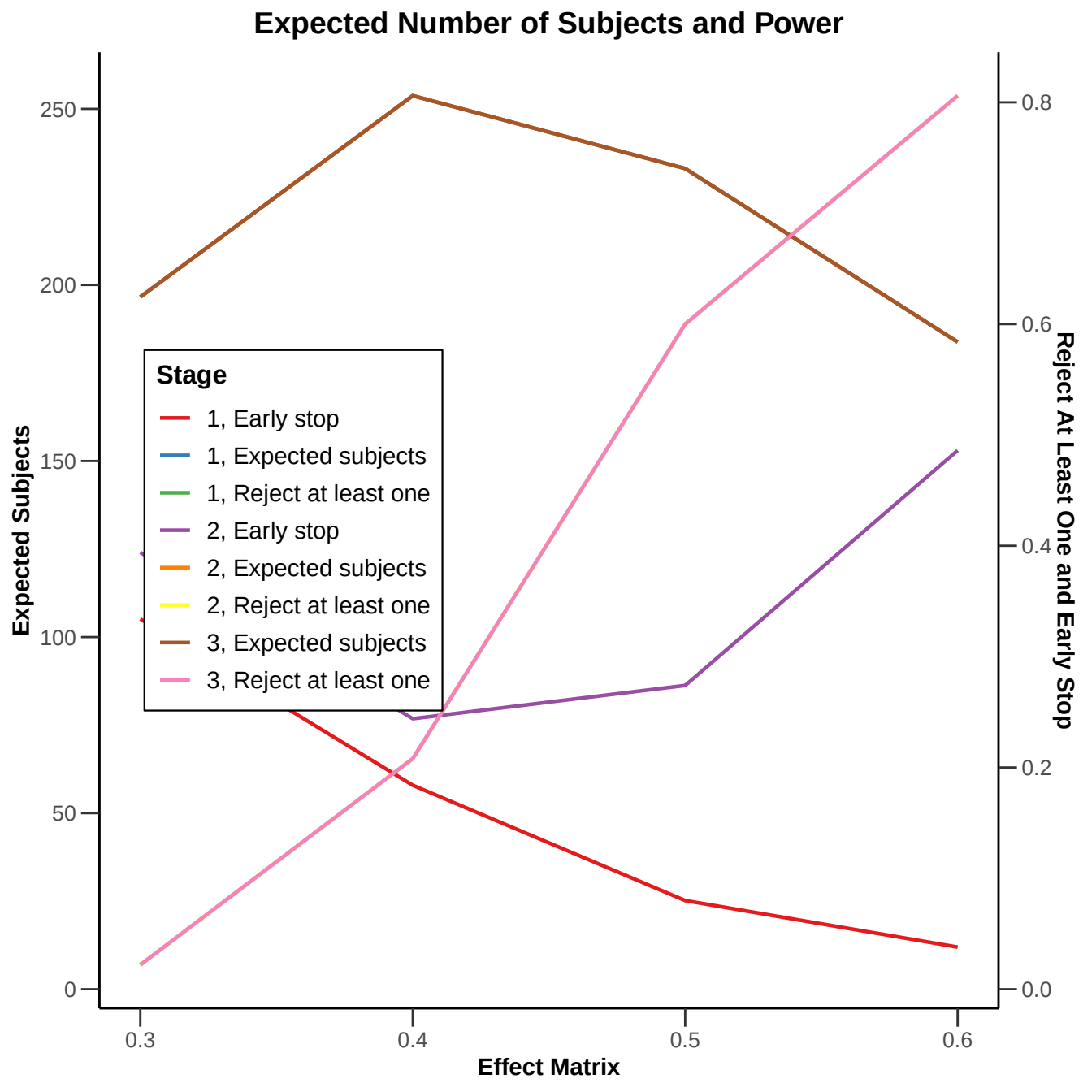

Overall Success
0.8
0.6
0.4
0.2
0.0
Overall Success
0.3
0.4
0.5
0.6
Maximum Effect

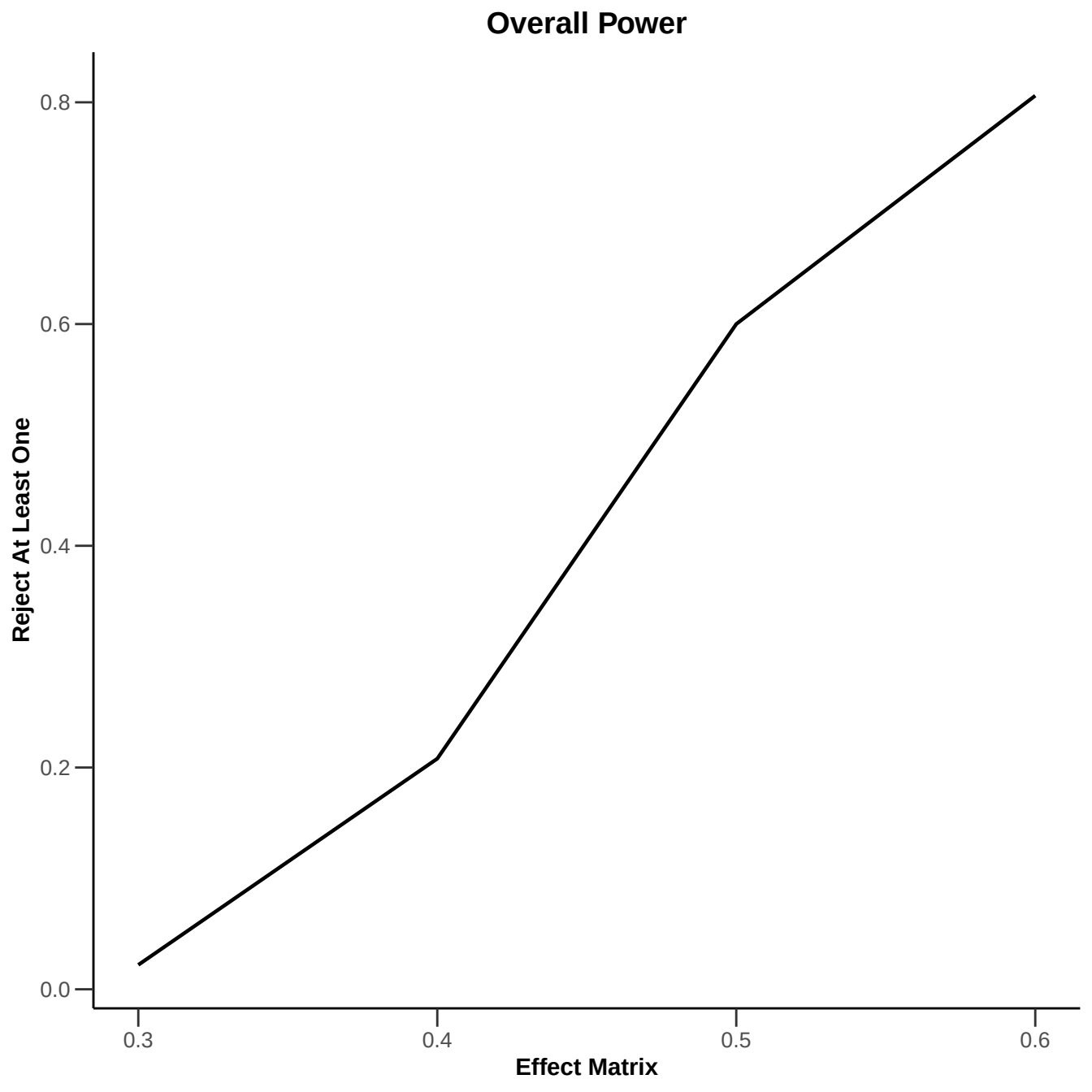

Success per Stage
Stage
1
2
3
0.4
0.3
0.2
0.1
0.0
Success
0.3
0.4
0.5
0.6
Maximum Effect

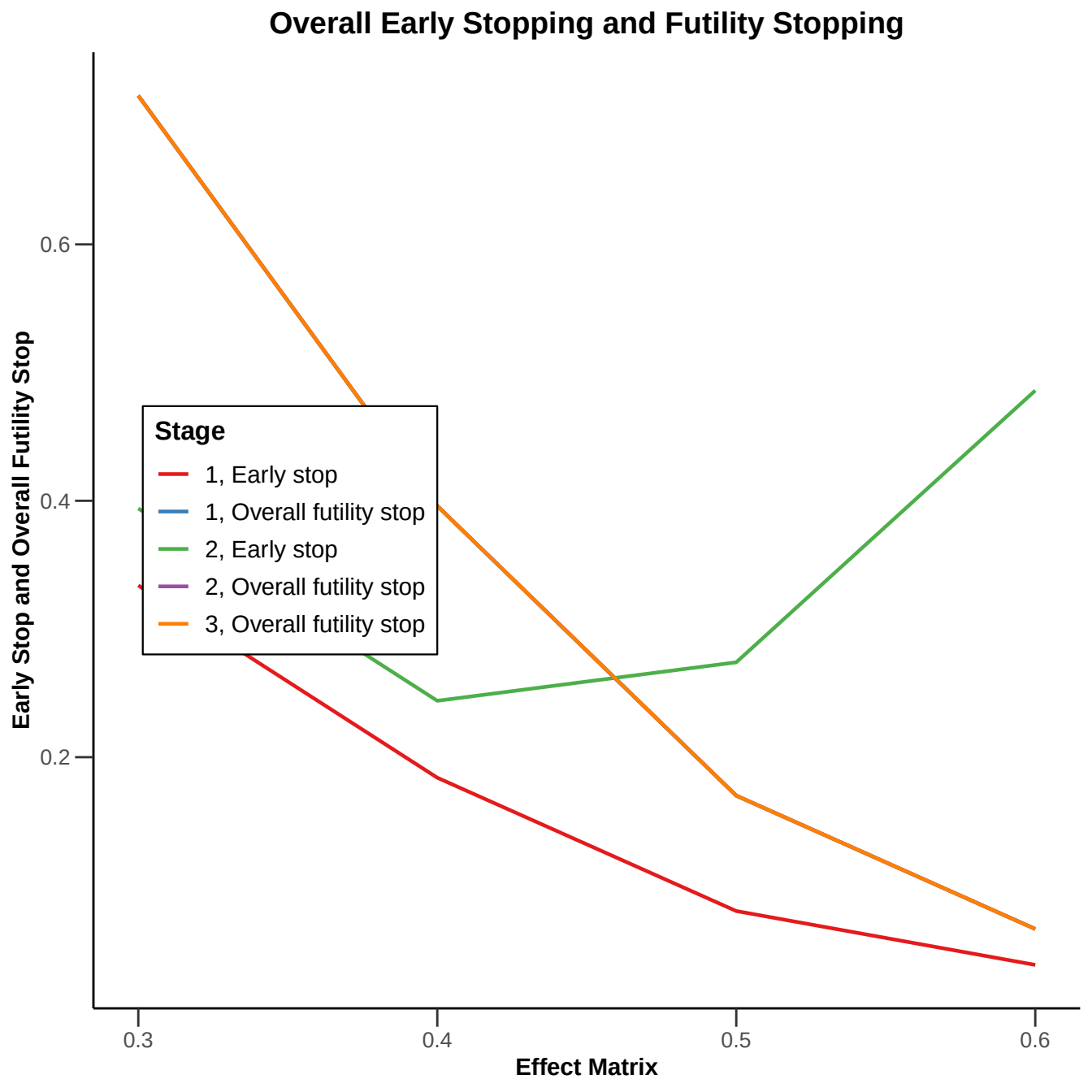

Selected Arms per Stage
Arm, Stage
1, 2
1, 3
2, 2
2, 3
3, 2
3, 3
4, 2
4, 3
Selected Arms
0.4
0.3
0.2
0.1
0.3
0.4
0.5
0.6
Maximum Effect

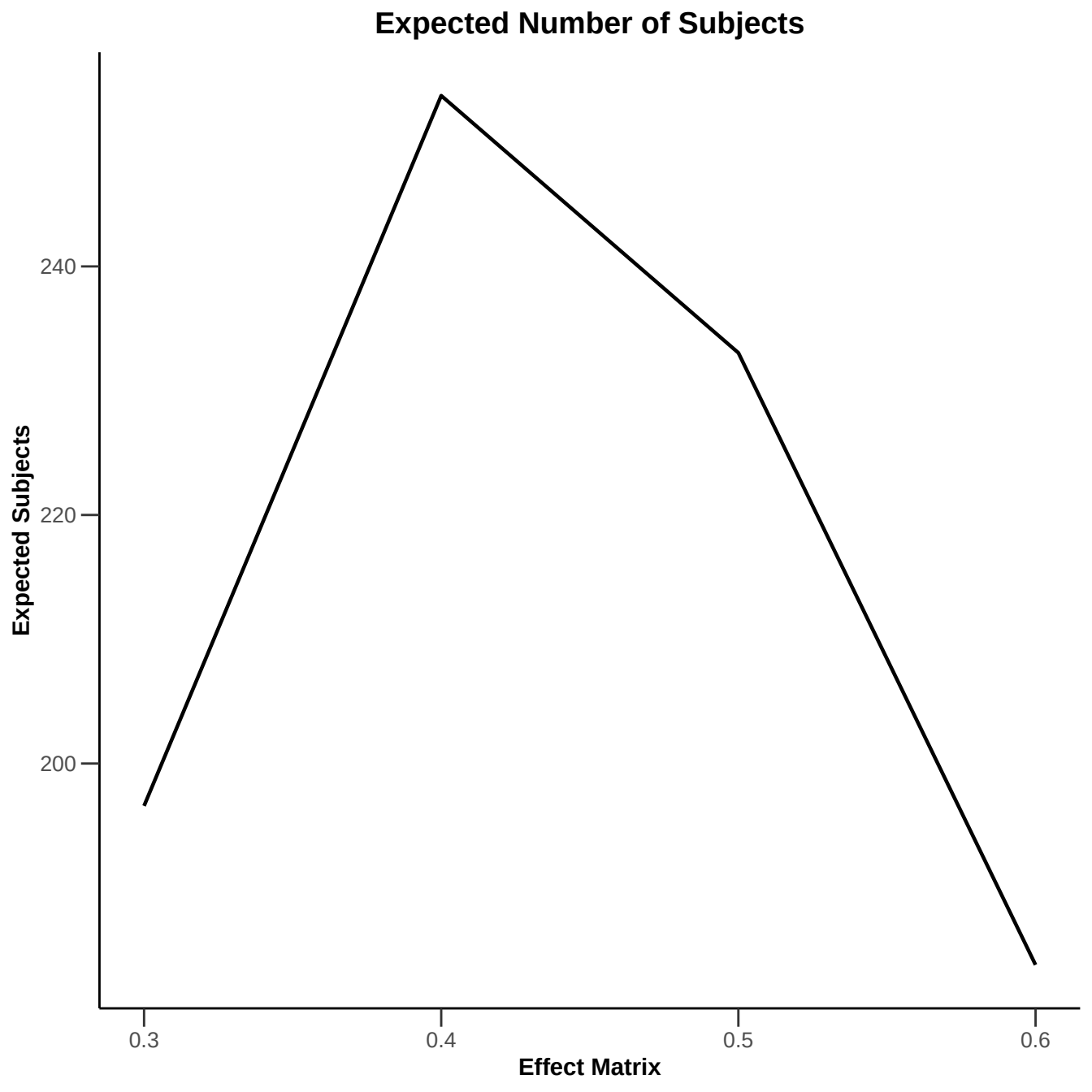

Rejected Arms per Stage
Arm, Stage
1, 1
1, 2
1, 3
2, 1
2, 2
2, 3
3, 1
3, 2
3, 3
4, 1
4, 2
4, 3
Rejected Arms
0.0
0.1
0.2
0.3
0.3
0.4
0.5
0.6
Maximum Effect

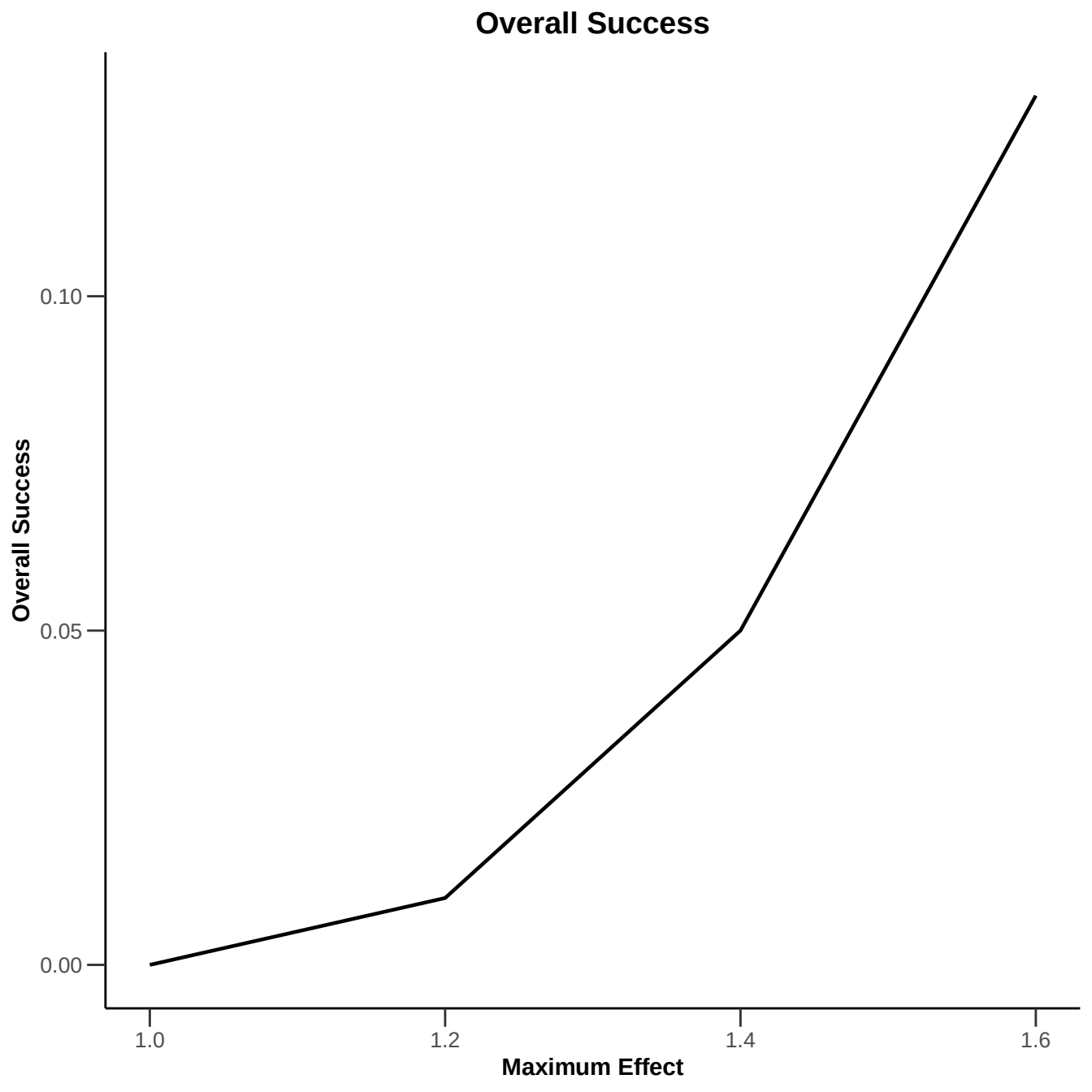

Overall Power and Early Stopping
Early stop, stage 1
Early stop, stage 2
Overall futility stop
Reject at least one
0.8
0.6
0.4
0.2
0.0
0.3
0.4
0.5
0.6
Maximum Effect

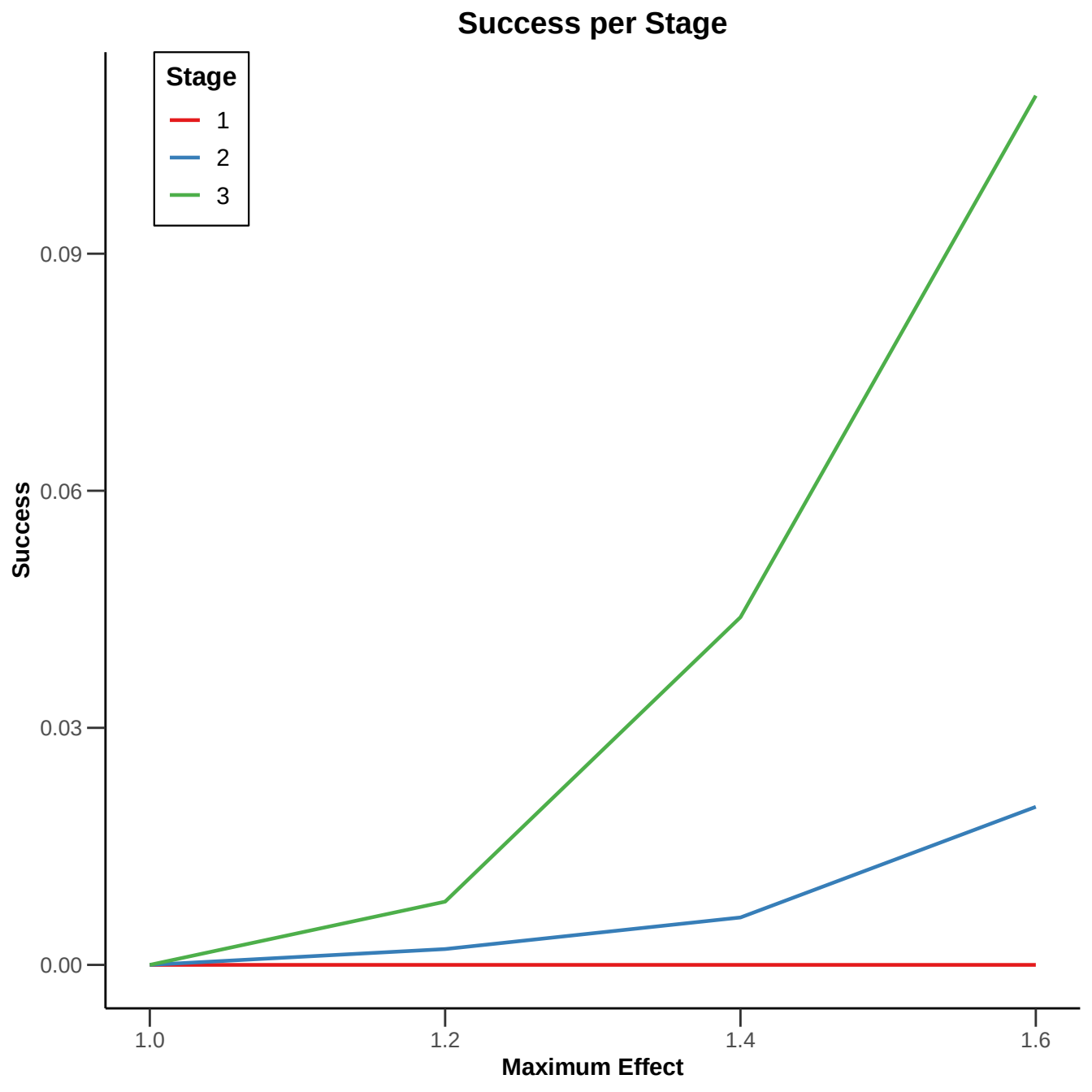

Expected Number of Subjects and Power
Expected Subjects
Reject At Least One and Early Stop
Effect Matrix
250
200
150
100
50
0
0.8
0.6
0.4
0.2
0.0
0.3
0.4
0.5
0.6
Stage
1, Early stop
1, Expected subjects
1, Reject at least one
2, Early stop
2, Expected subjects
2, Reject at least one
3, Expected subjects
3, Reject at least one

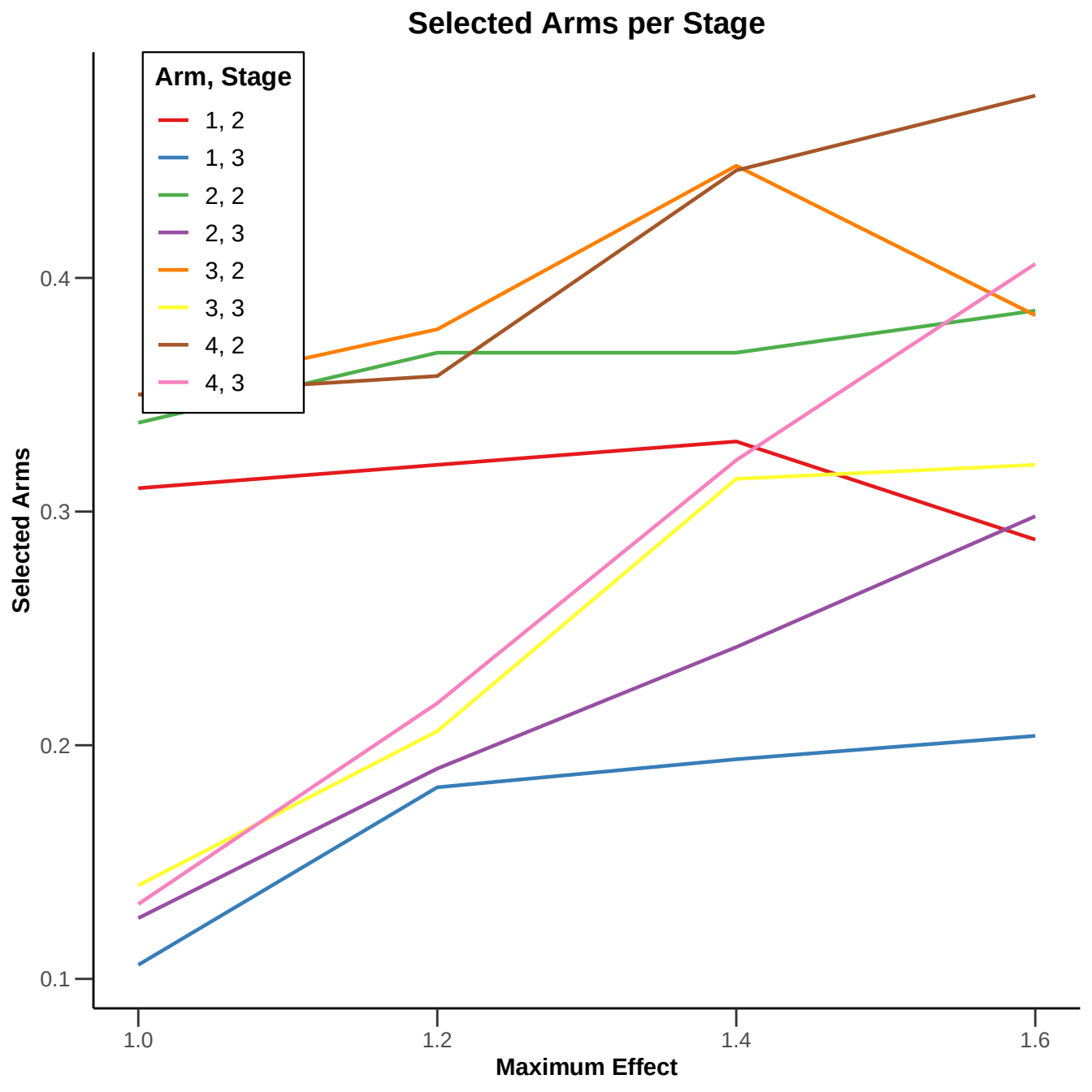

Overall Power
Reject At Least One
0.0
0.2
0.4
0.6
0.8
0.3
0.4
0.5
0.6
Effect Matrix

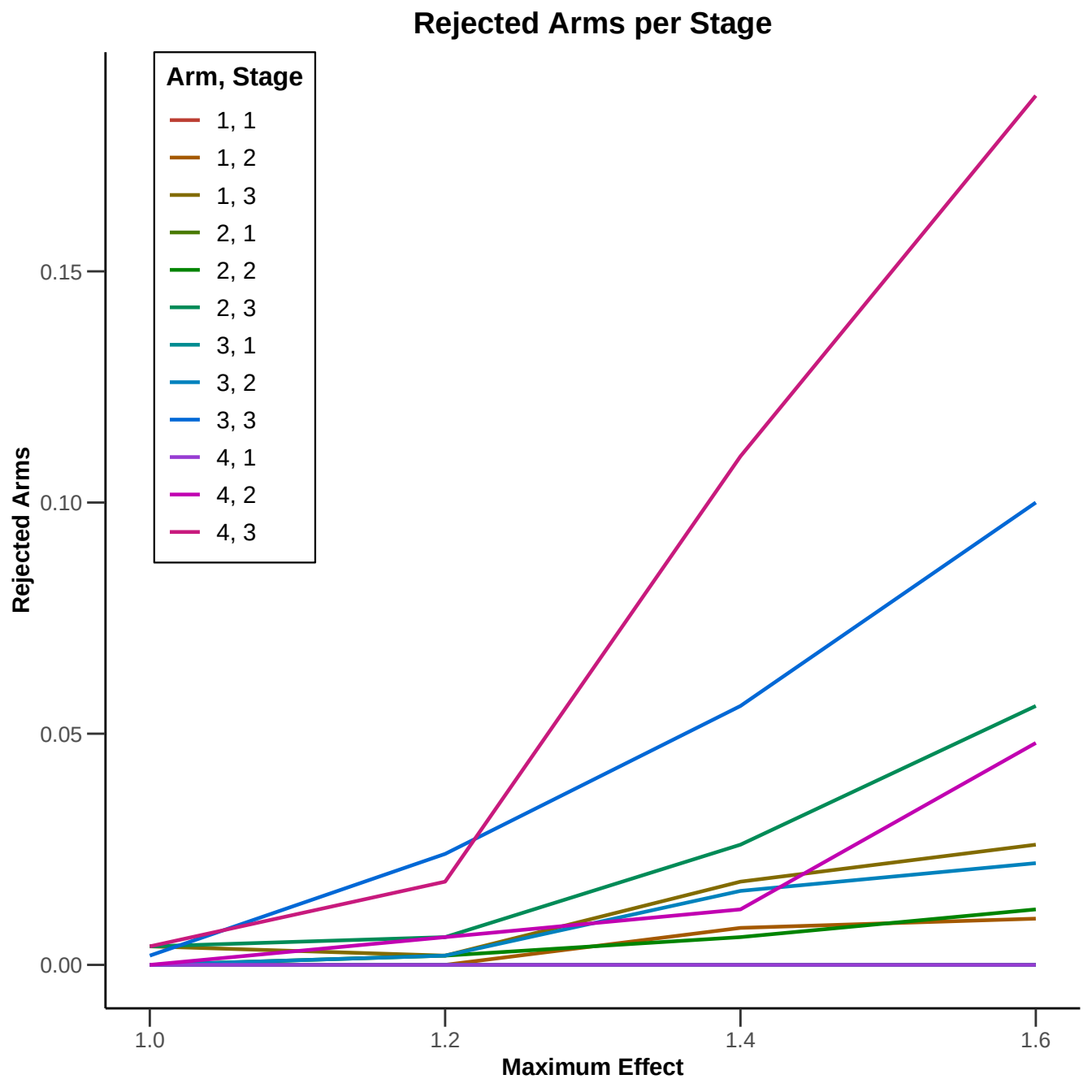

Overall Early Stopping and Futility Stopping
Early Stop and Overall Futility Stop
0.6
0.4
0.2
Stage
1, Early stop
1, Overall futility stop
2, Early stop
2, Overall futility stop
3, Overall futility stop
0.3
0.4
0.5
0.6
Effect Matrix

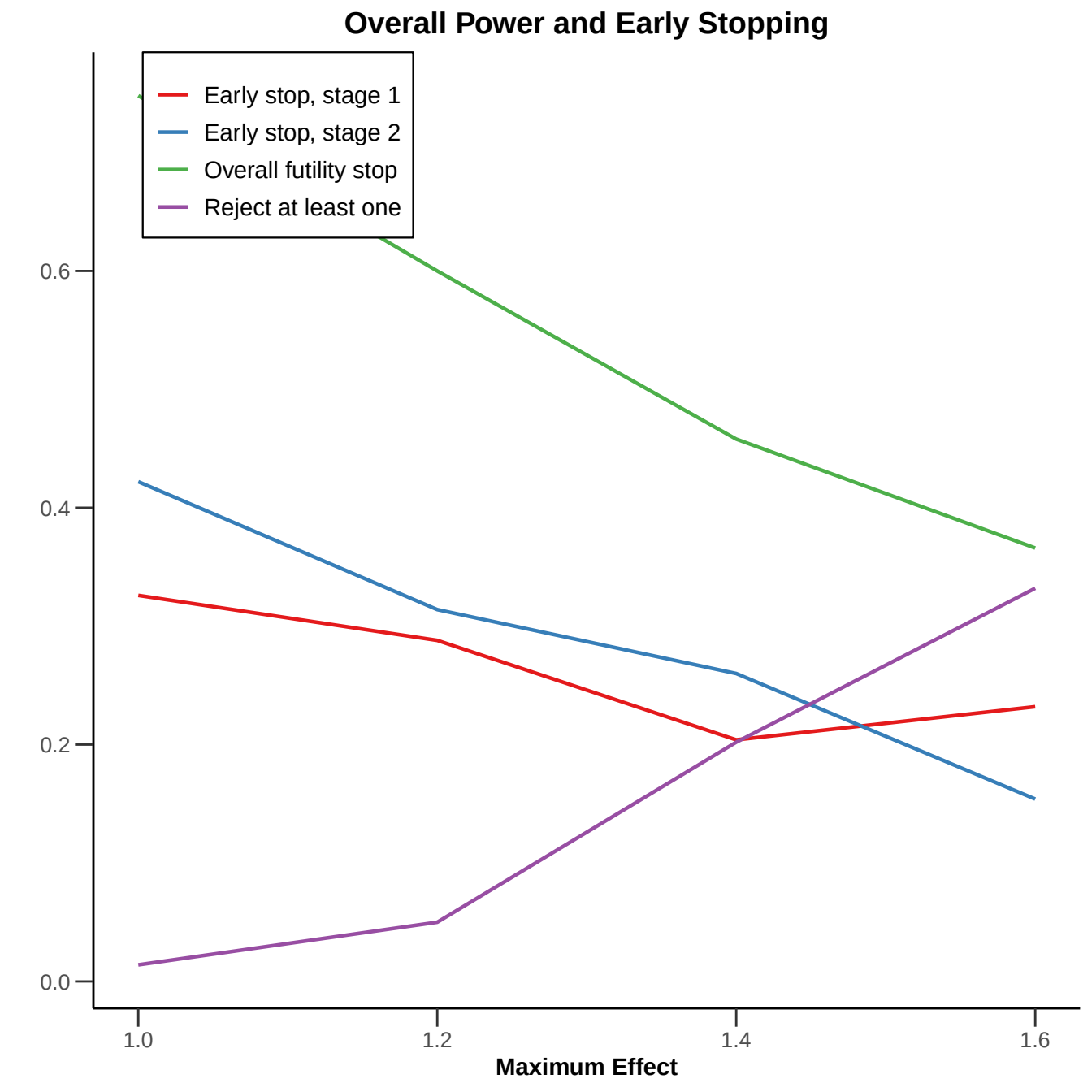

Expected Number of Subjects
Expected Subjects
240
220
200
0.3
0.4
0.5
0.6
Effect Matrix

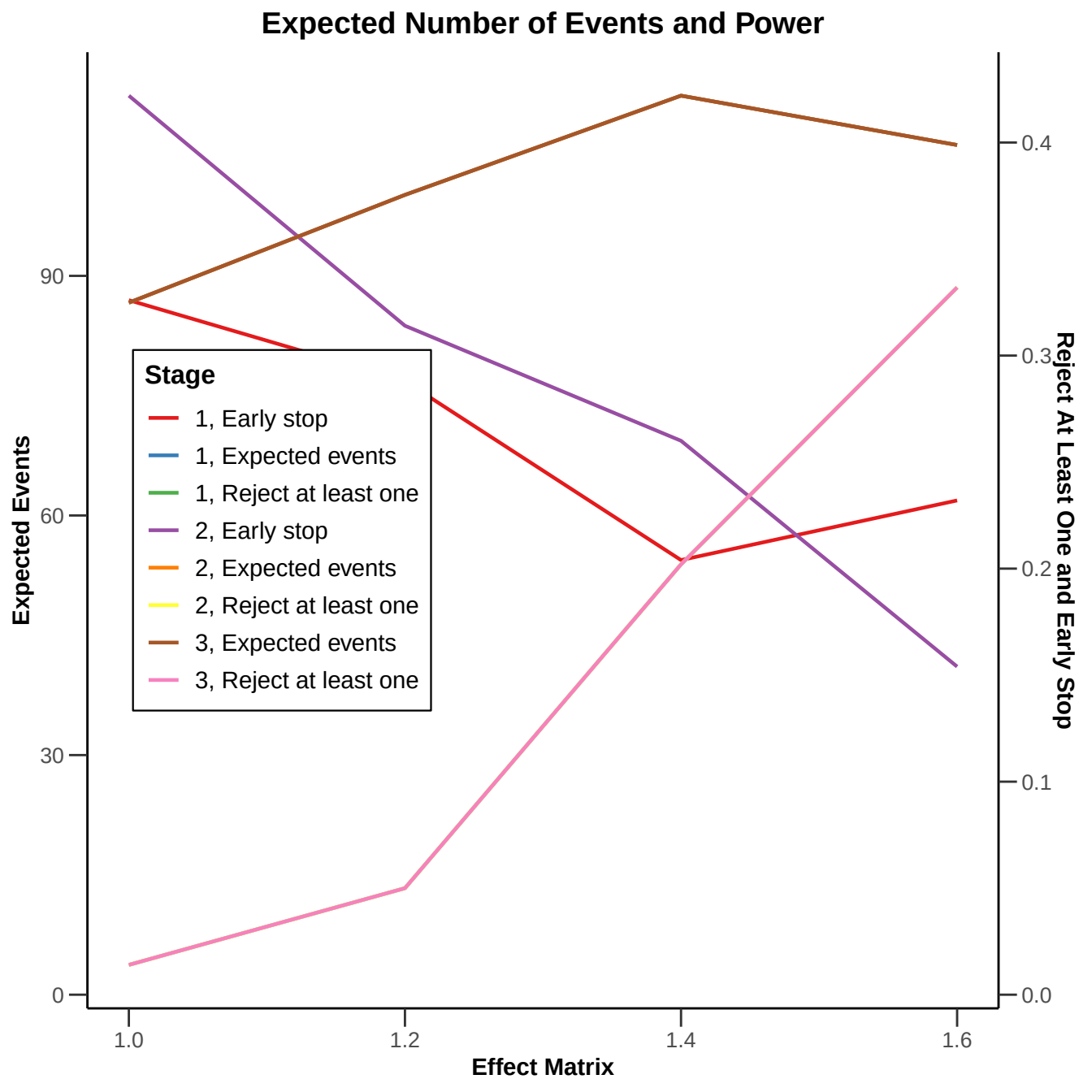

Overall Success
0.10
0.05
0.00
Overall Success
1.0
1.2
1.4
1.6
Maximum Effect

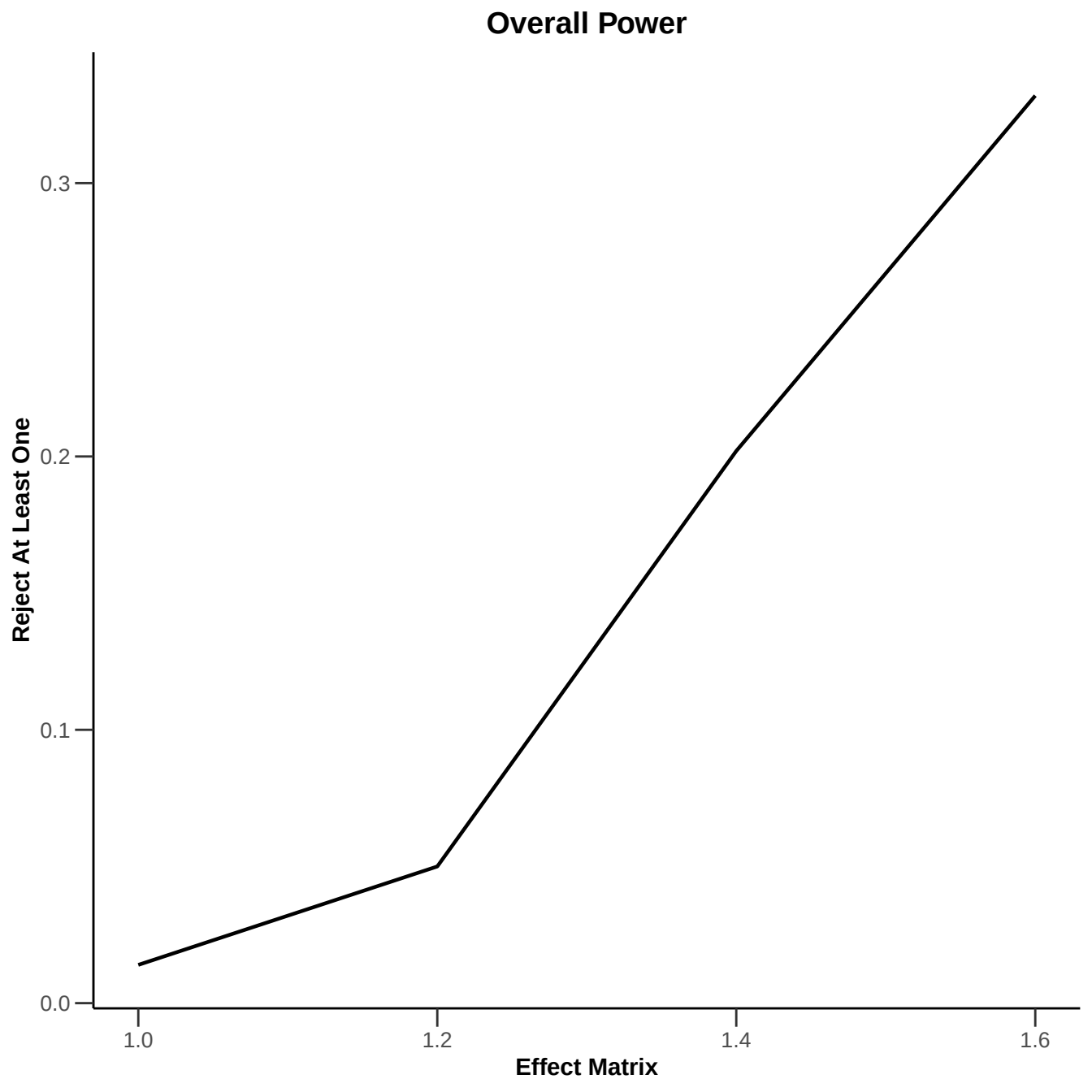

Success per Stage
Stage
1
2
3
0.09
0.06
0.03
0.00
Success
1.0
1.2
1.4
1.6
Maximum Effect

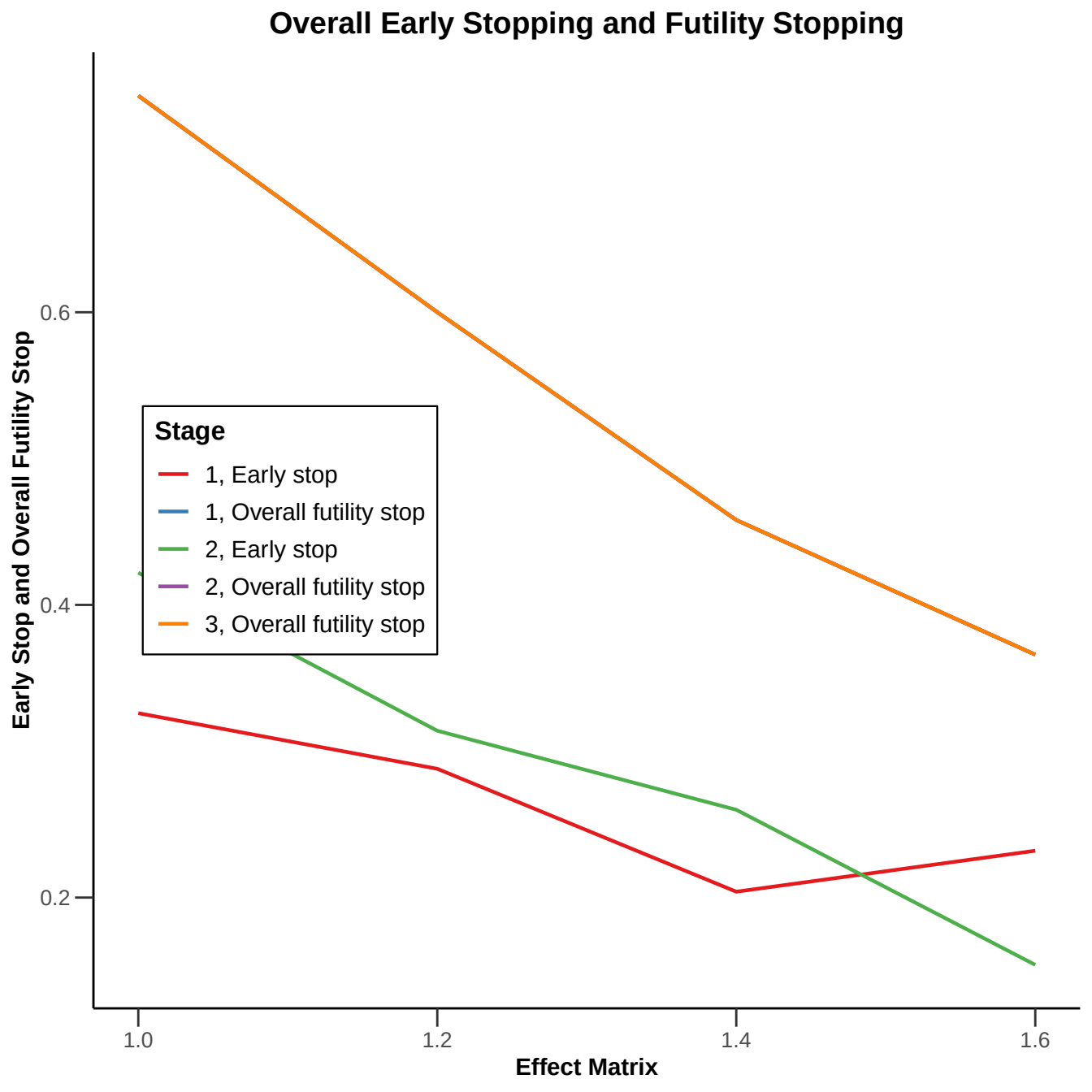

Selected Arms per Stage
Arm, Stage
1, 2
1, 3
2, 2
2, 3
3, 2
3, 3
4, 2
4, 3
Selected Arms
0.4
0.3
0.2
0.1
1.0
1.2
1.4
1.6
Maximum Effect

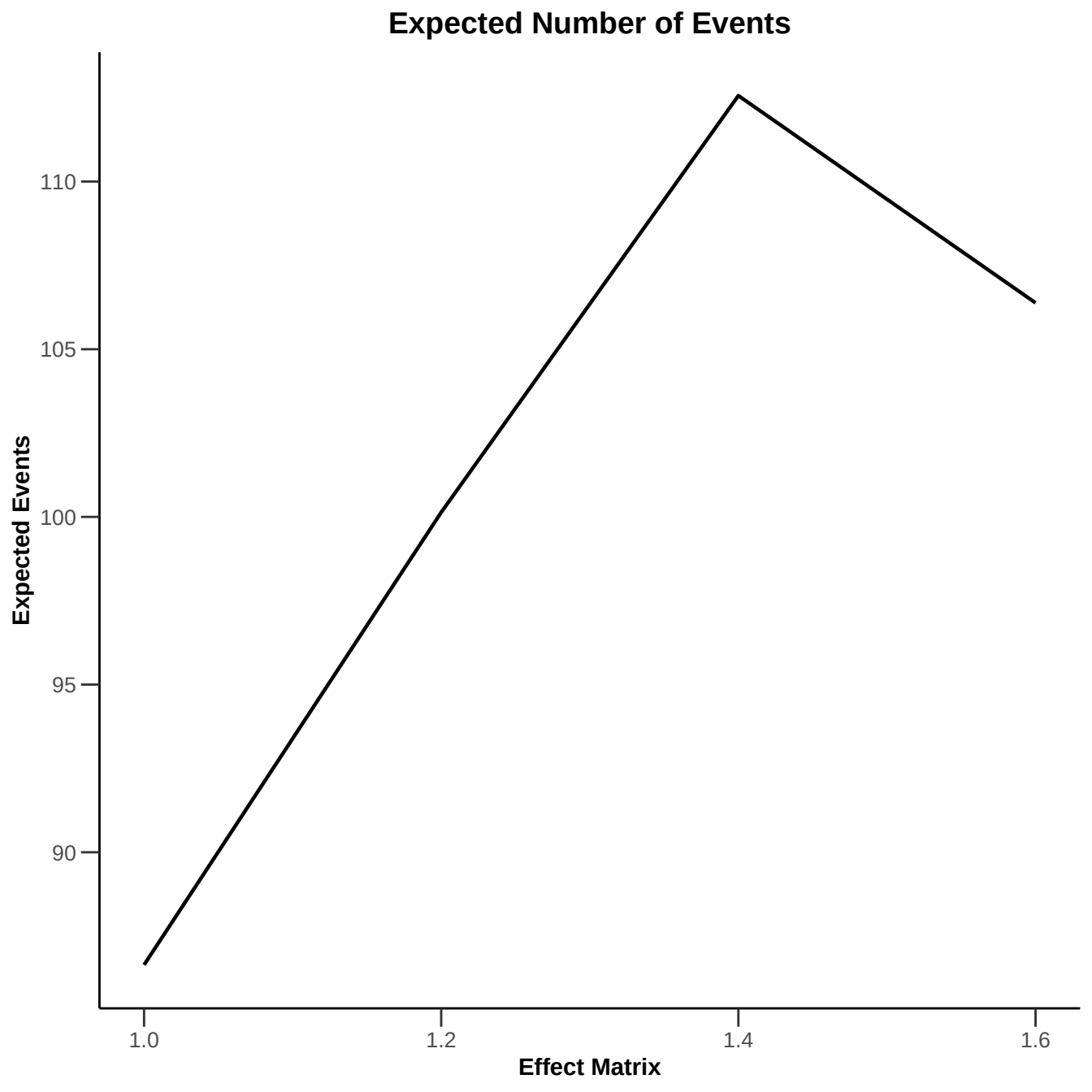

Rejected Arms per Stage
Arm, Stage
1, 1
1, 2
1, 3
2, 1
2, 2
2, 3
3, 1
3, 2
3, 3
4, 1
4, 2
4, 3
Rejected Arms
0.00
0.05
0.10
0.15
1.0
1.2
1.4
1.6
Maximum Effect

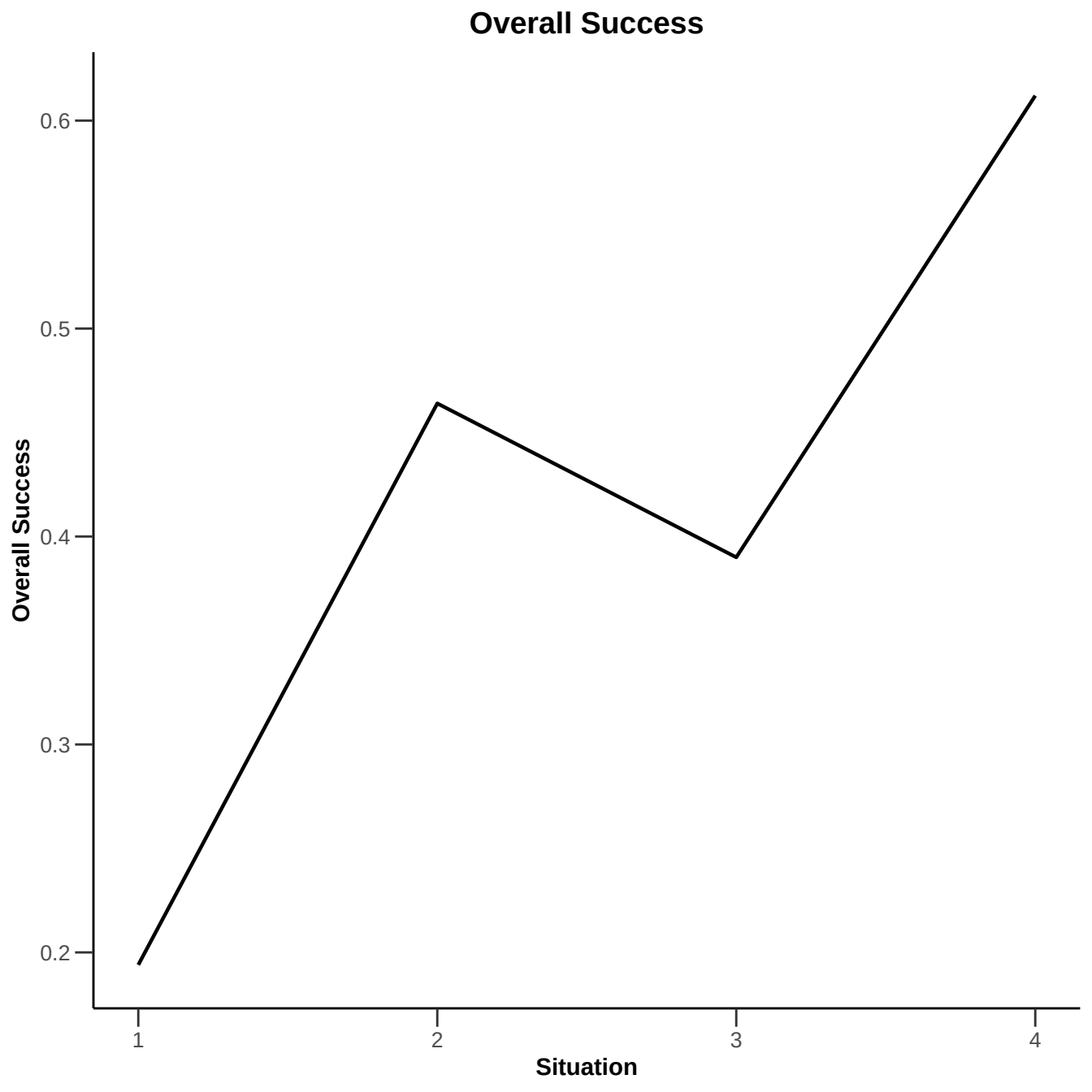

Overall Power and Early Stopping
Early stop, stage 1
Early stop, stage 2
Overall futility stop
Reject at least one
0.6
0.4
0.2
0.0
1.0
1.2
1.4
1.6
Maximum Effect

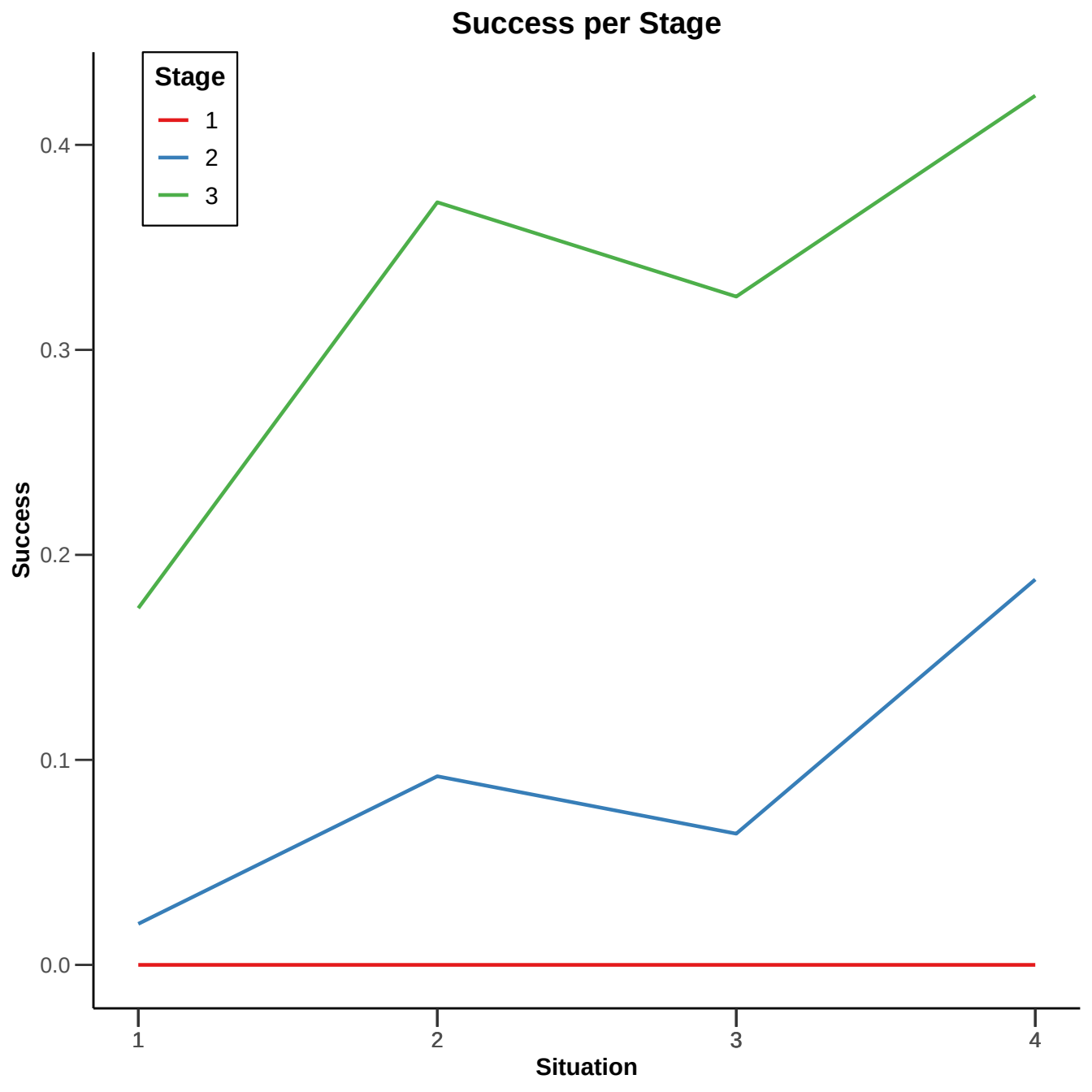

Expected Number of Events and Power
Expected Events
Reject At Least One and Early Stop
Effect Matrix
Stage
1, Early stop
1, Expected events
1, Reject at least one
2, Early stop
2, Expected events
2, Reject at least one
3, Expected events
3, Reject at least one
0
30
60
90
0.0
0.1
0.2
0.3
0.4
1.0
1.2
1.4
1.6

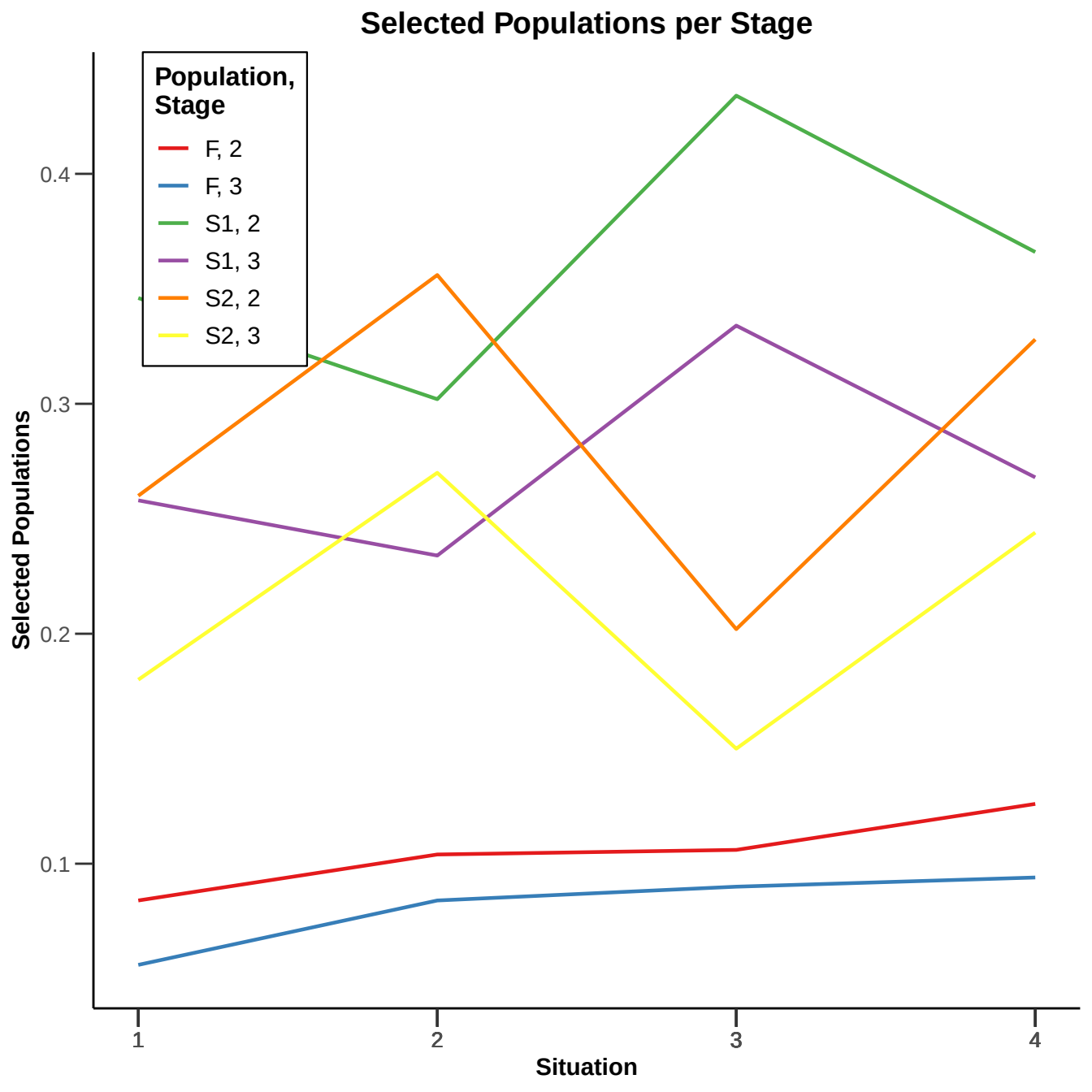

Overall Power
Reject At Least One
0.0
0.1
0.2
0.3
1.0
1.2
1.4
1.6
Effect Matrix

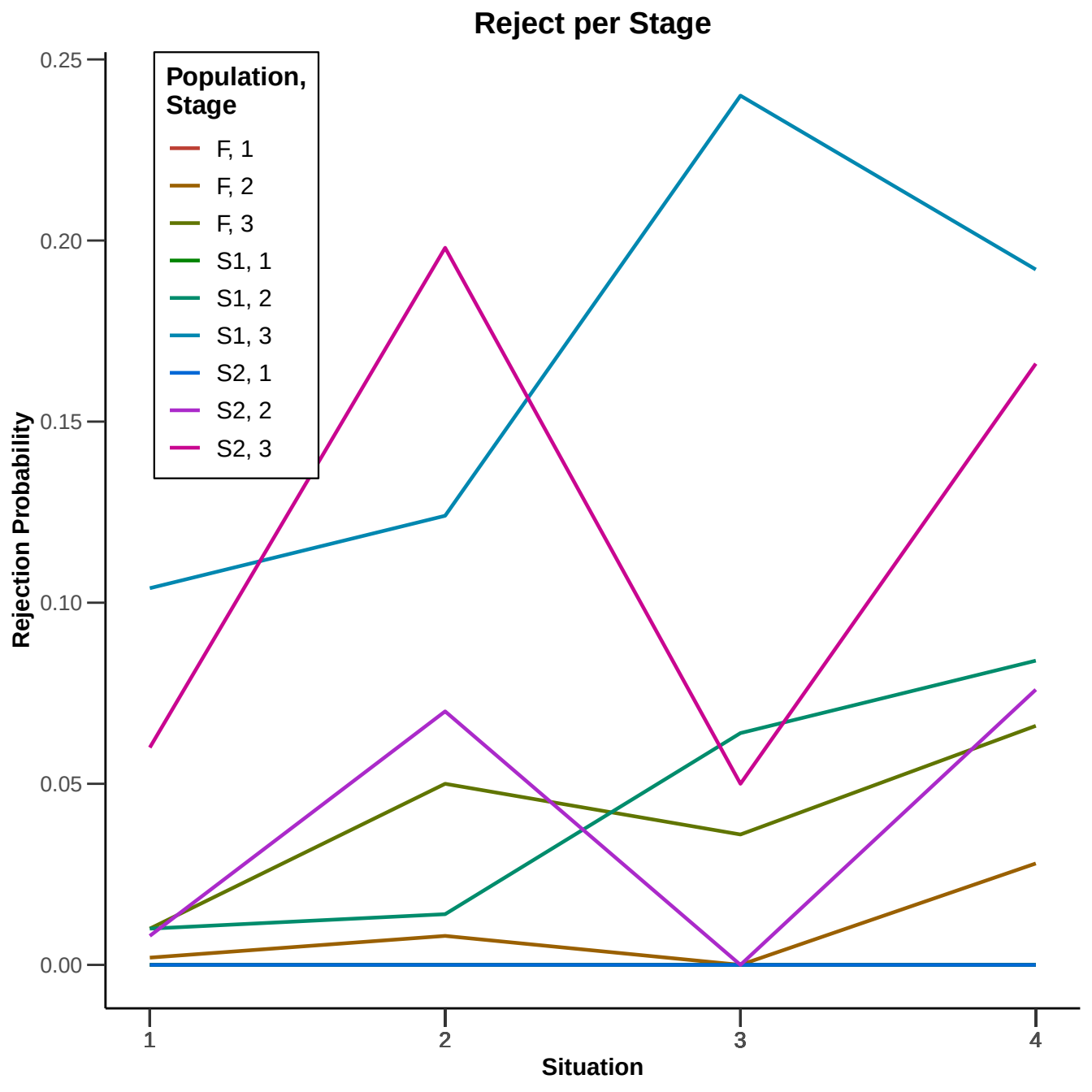

Overall Early Stopping and Futility Stopping
Early Stop and Overall Futility Stop
0.6
0.4
0.2
Stage
1, Early stop
1, Overall futility stop
2, Early stop
2, Overall futility stop
3, Overall futility stop
1.0
1.2
1.4
1.6
Effect Matrix

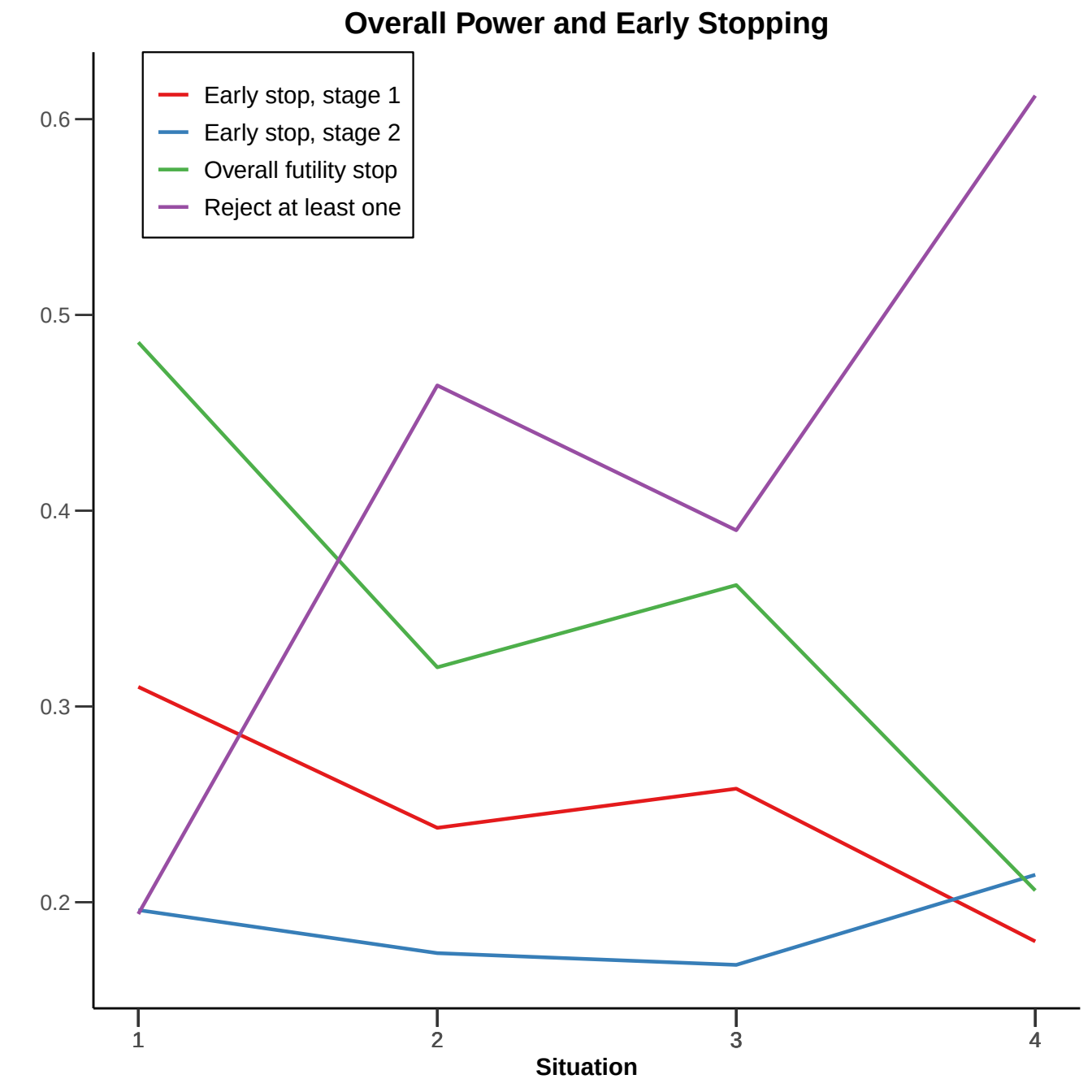

Expected Number of Events
Expected Events
110
105
100
95
90
1.0
1.2
1.4
1.6
Effect Matrix

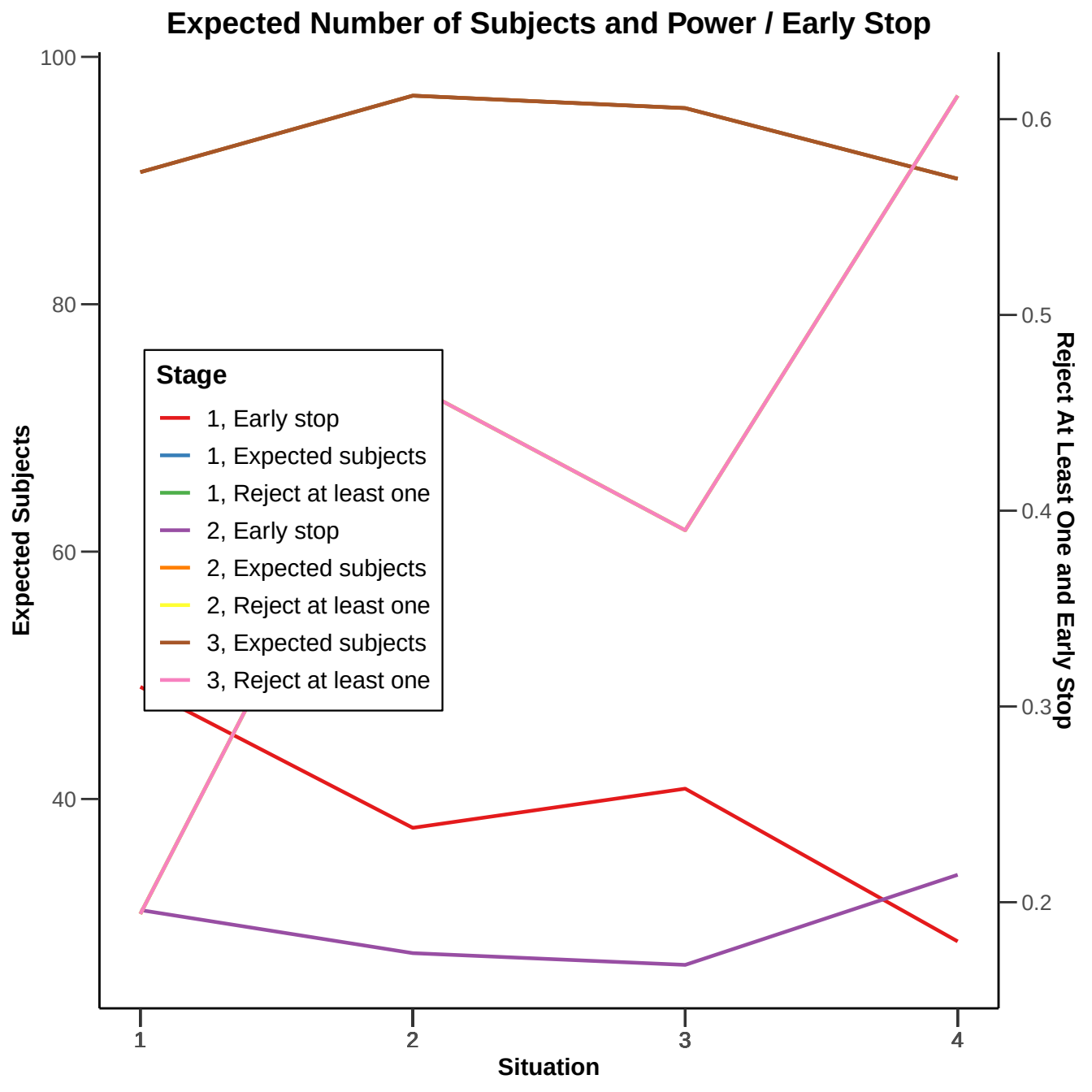

Overall Success
0.6
0.5
0.4
0.3
0.2
Overall Success
1
2
3
4
Situation

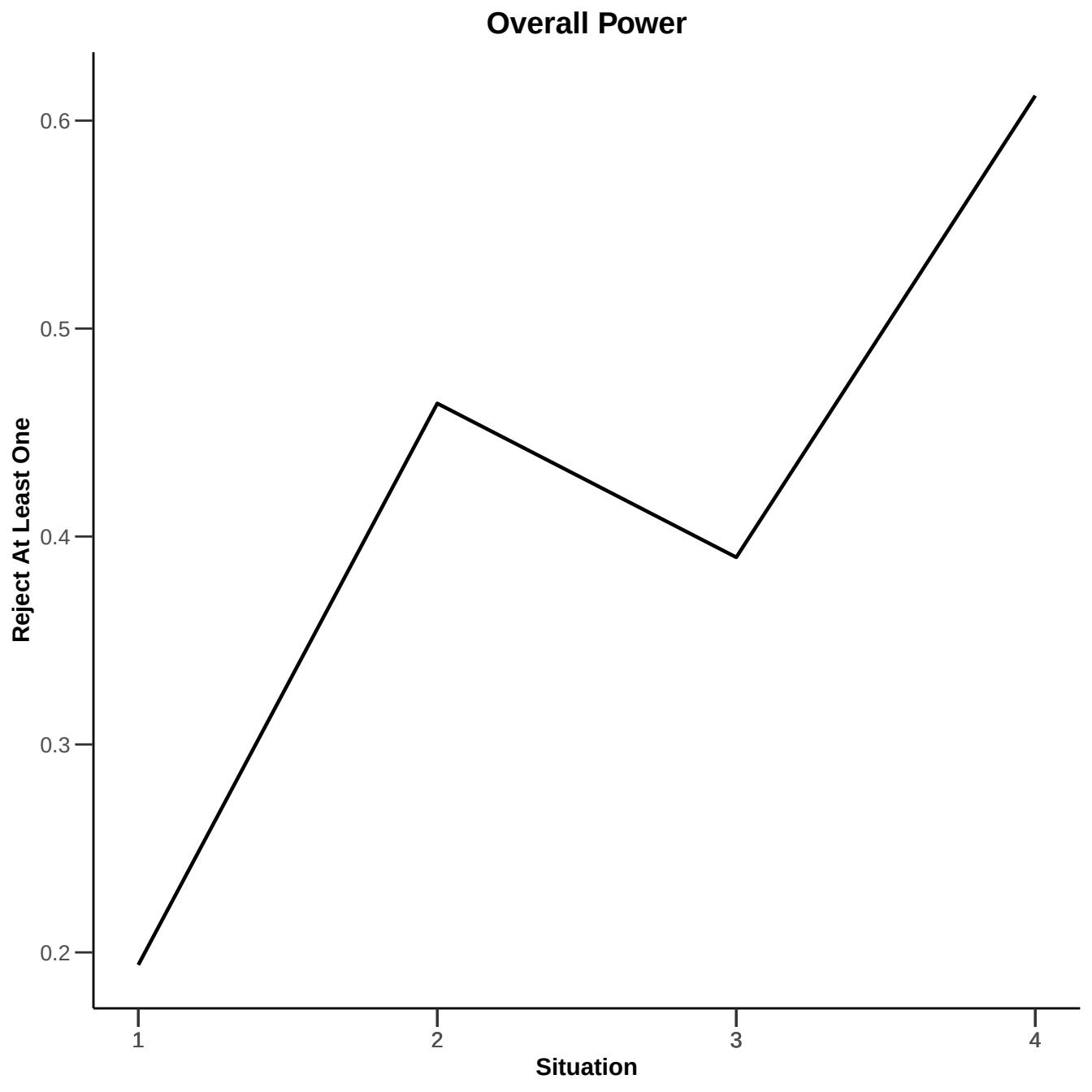

Success per Stage
Stage
1
2
3
0.4
0.3
0.2
0.1
0.0
Success
1
2
3
4
Situation

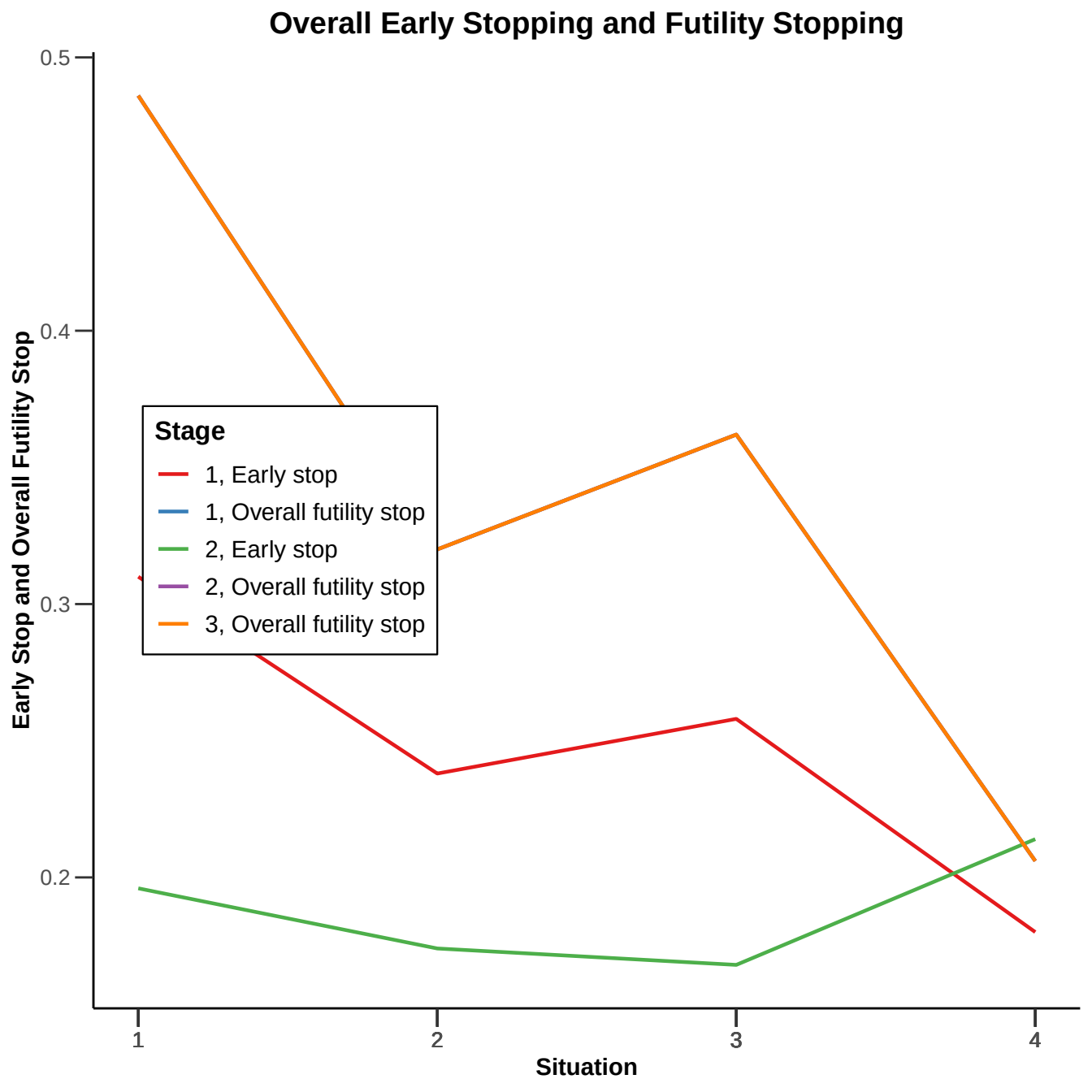

Selected Populations per Stage
Population, Stage
F, 2
F, 3
S1, 2
S1, 3
S2, 2
S2, 3
0.4
0.3
0.2
0.1
Selected Populations
1
2
3
4
Situation

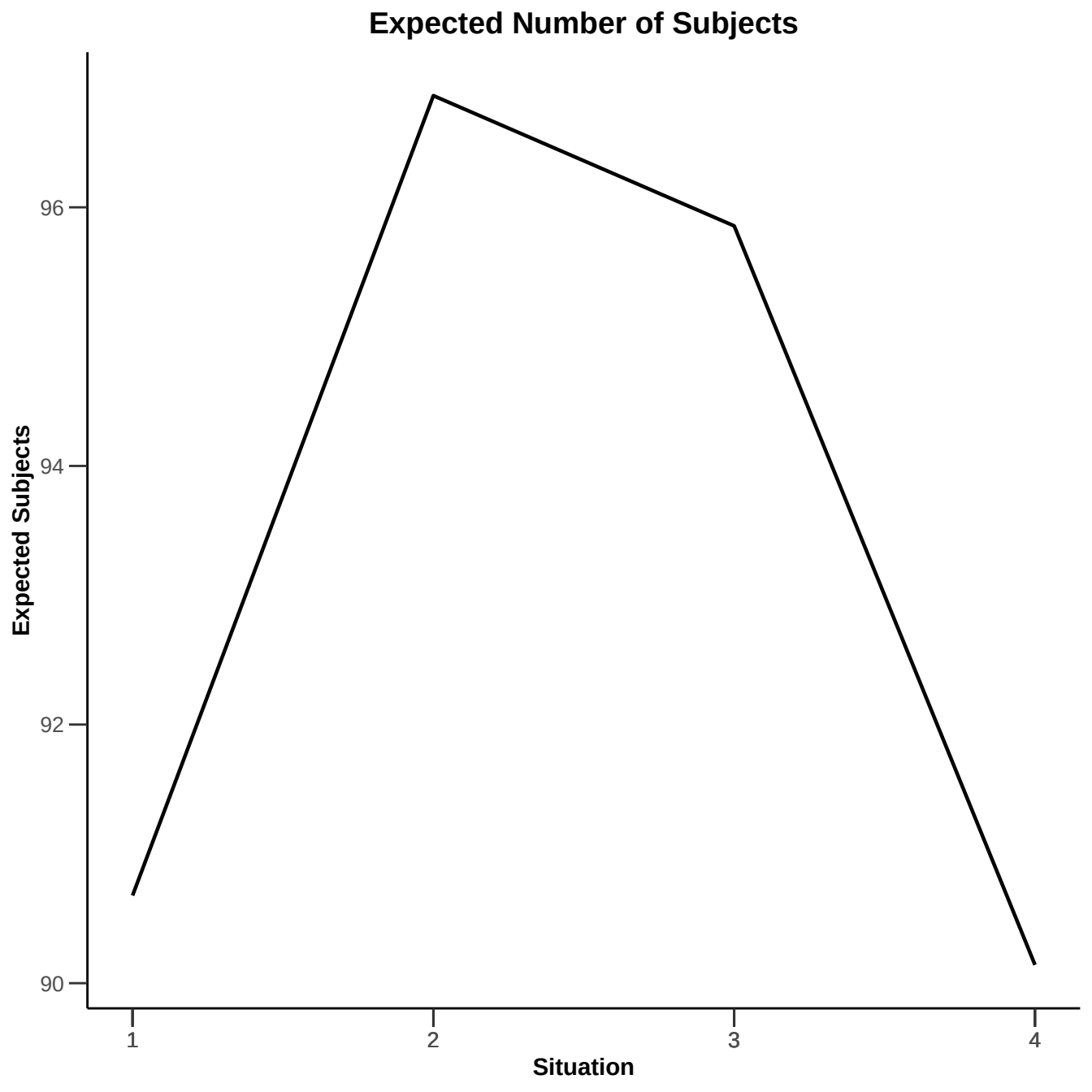

Reject per Stage
Population, Stage
F, 1
F, 2
F, 3
S1, 1
S1, 2
S1, 3
S2, 1
S2, 2
S2, 3
Rejection Probability
0.25
0.20
0.15
0.10
0.05
0.00
1
2
3
4
Situation

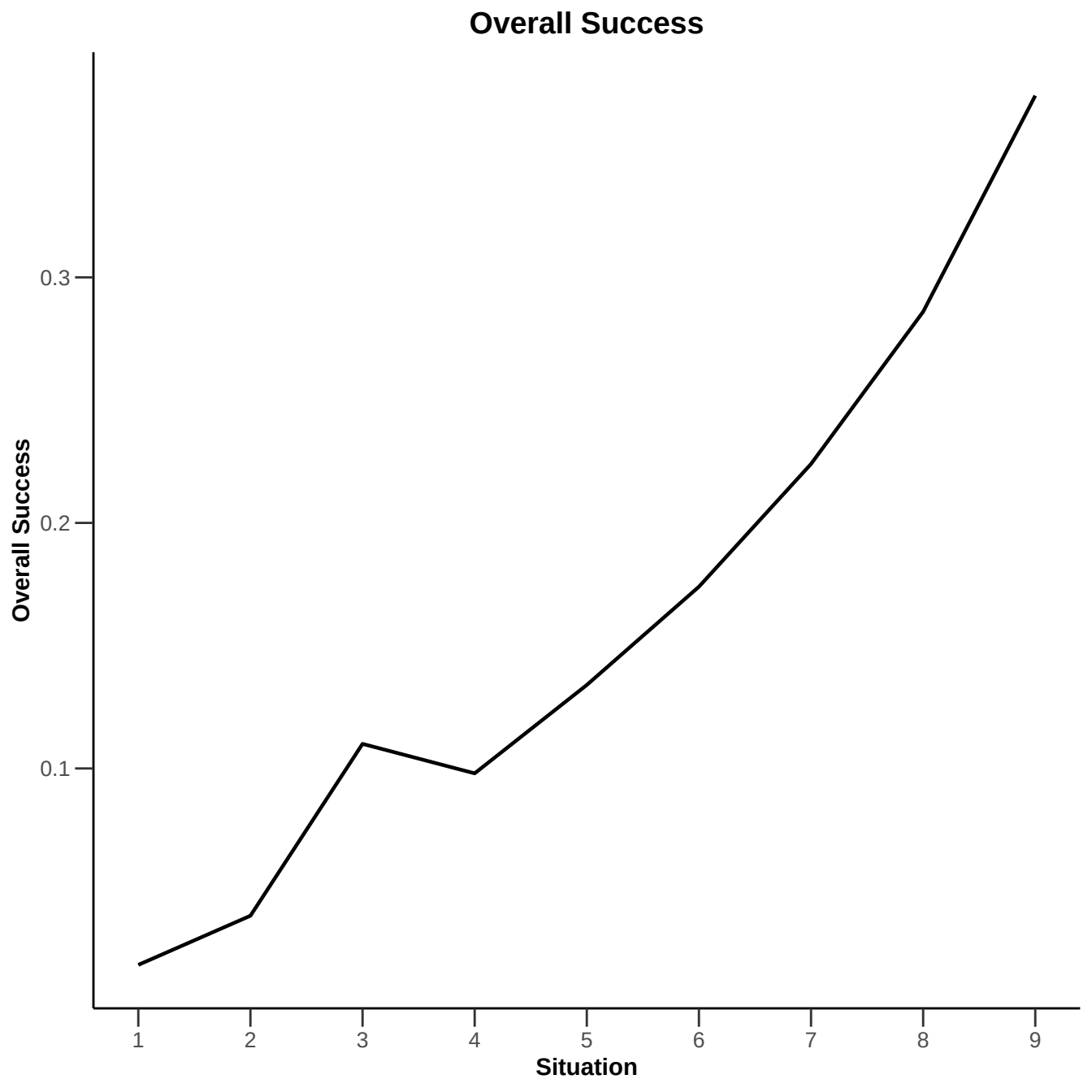

Overall Power and Early Stopping
Early stop, stage 1
Early stop, stage 2
Overall futility stop
Reject at least one
0.6
0.5
0.4
0.3
0.2
1
2
3
4
Situation

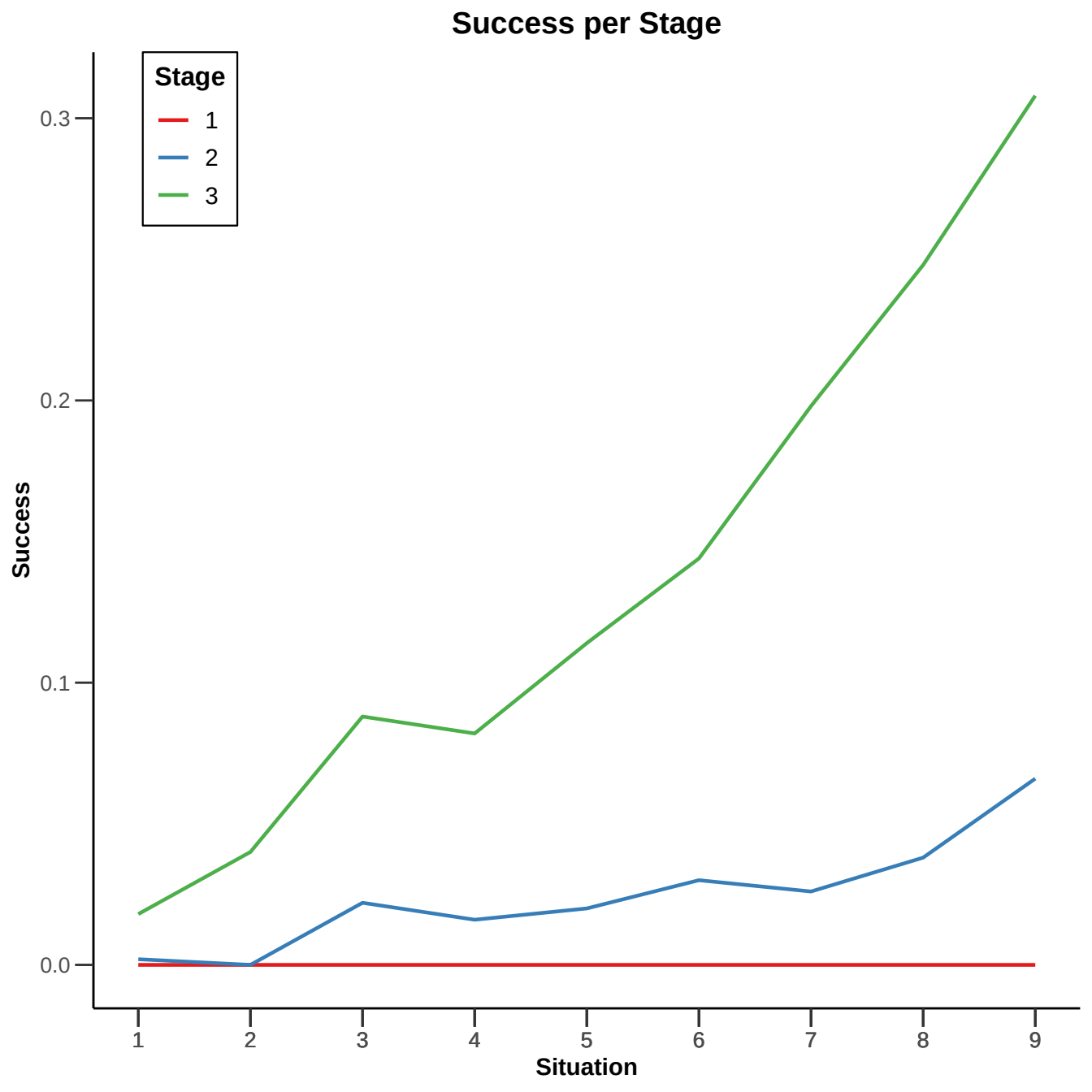

Expected Number of Subjects and Power / Early Stop
Expected Subjects
Reject At Least One and Early Stop
Situation
100
80
60
40
0.6
0.5
0.4
0.3
0.2
1
2
3
4
Stage
1, Early stop
1, Expected subjects
1, Reject at least one
2, Early stop
2, Expected subjects
2, Reject at least one
3, Expected subjects
3, Reject at least one

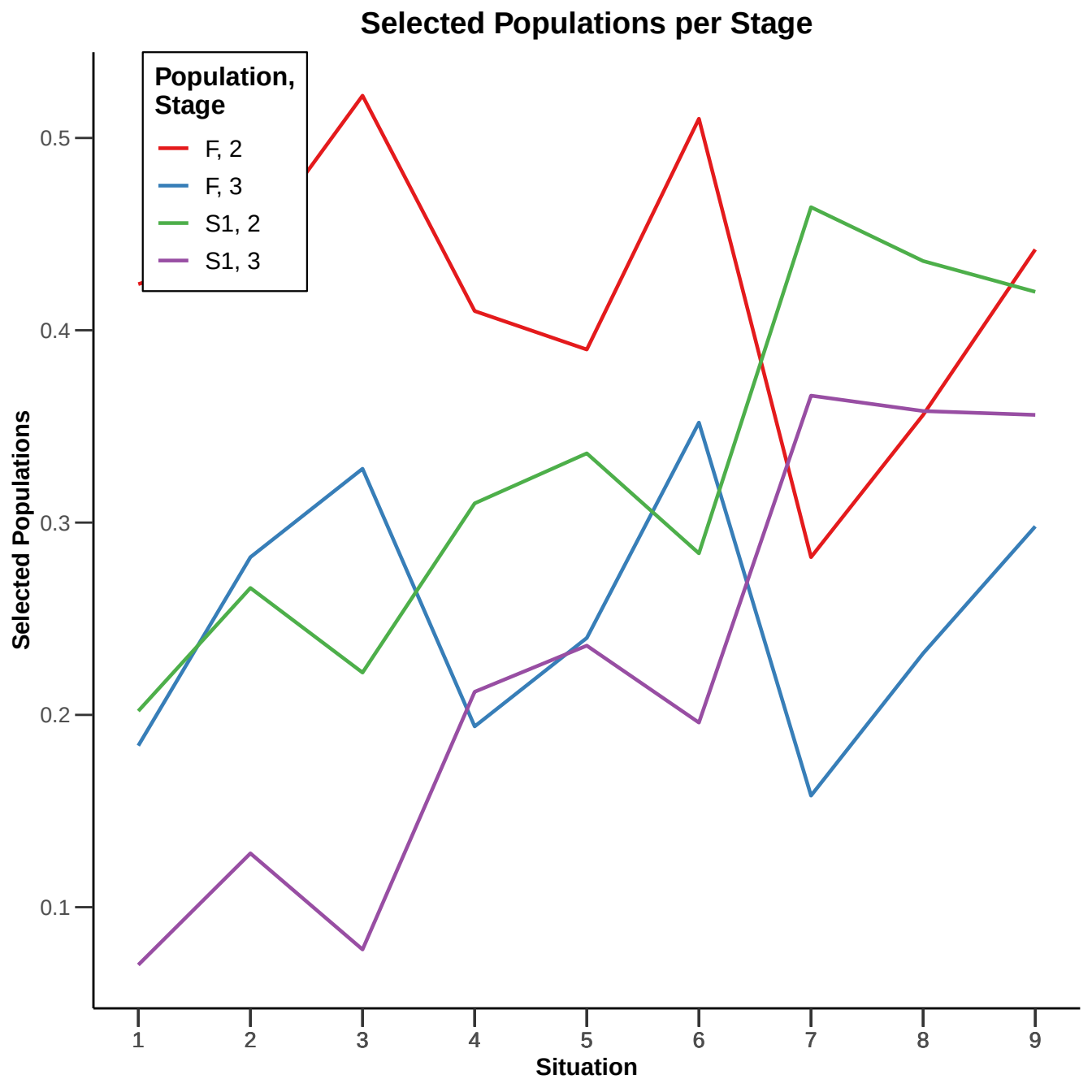

Overall Power
Reject At Least One
0.6
0.5
0.4
0.3
0.2
1
2
3
4
Situation

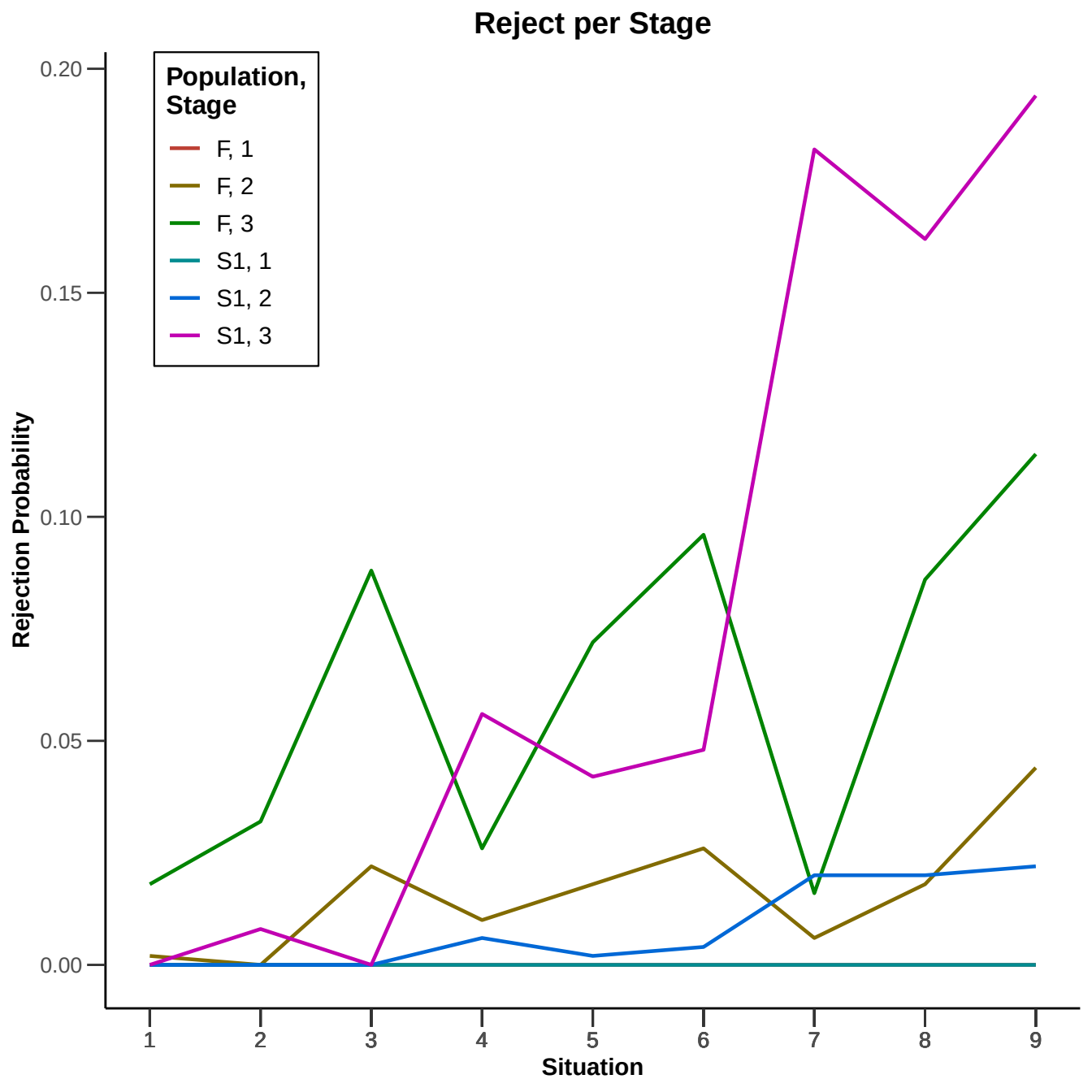

Overall Early Stopping and Futility Stopping
0.5
0.4
0.3
0.2
Early Stop and Overall Futility Stop
Stage
1, Early stop
1, Overall futility stop
2, Early stop
2, Overall futility stop
3, Overall futility stop
1
2
3
4
Situation

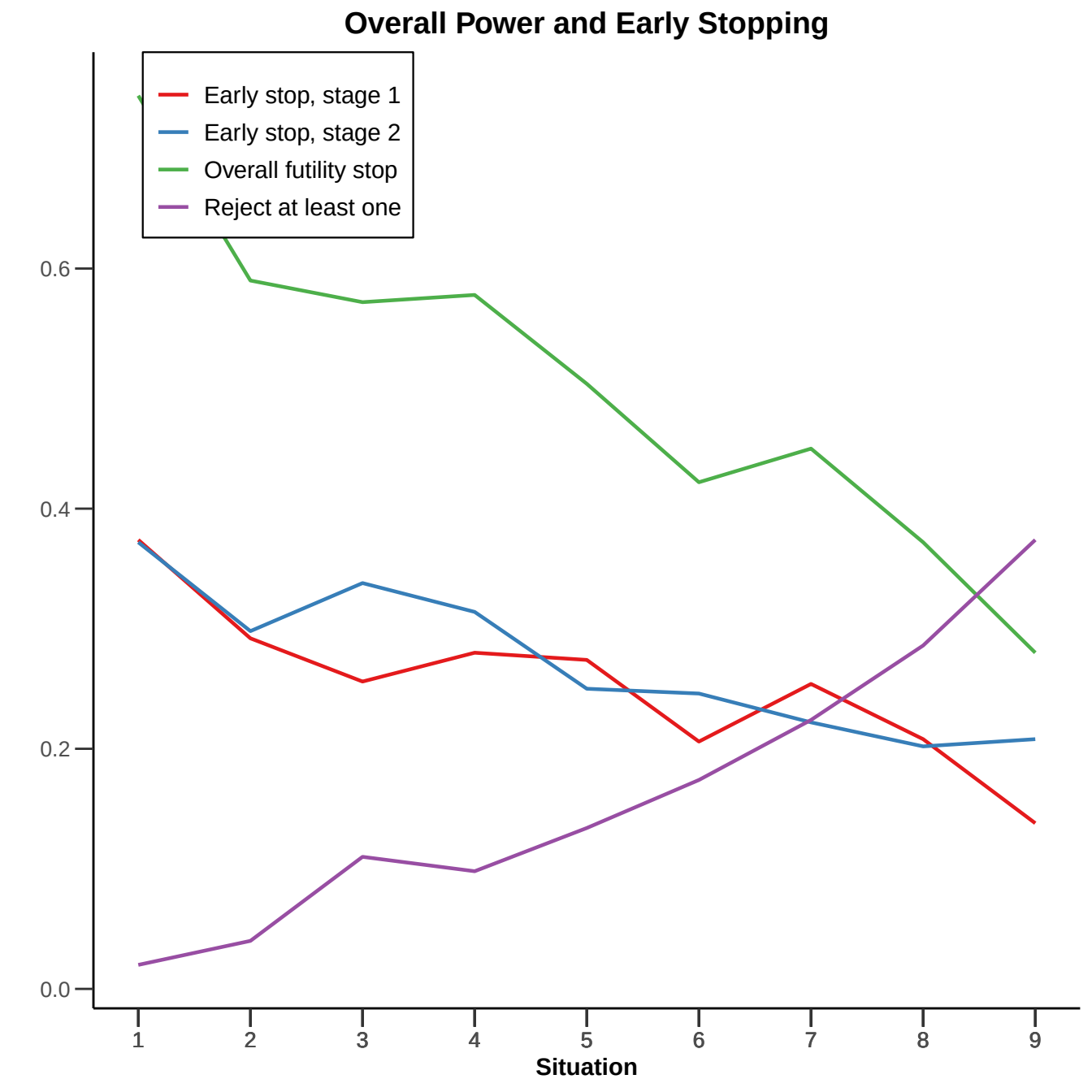

Expected Number of Subjects
Expected Subjects
96
94
92
90
1
2
3
4
Situation

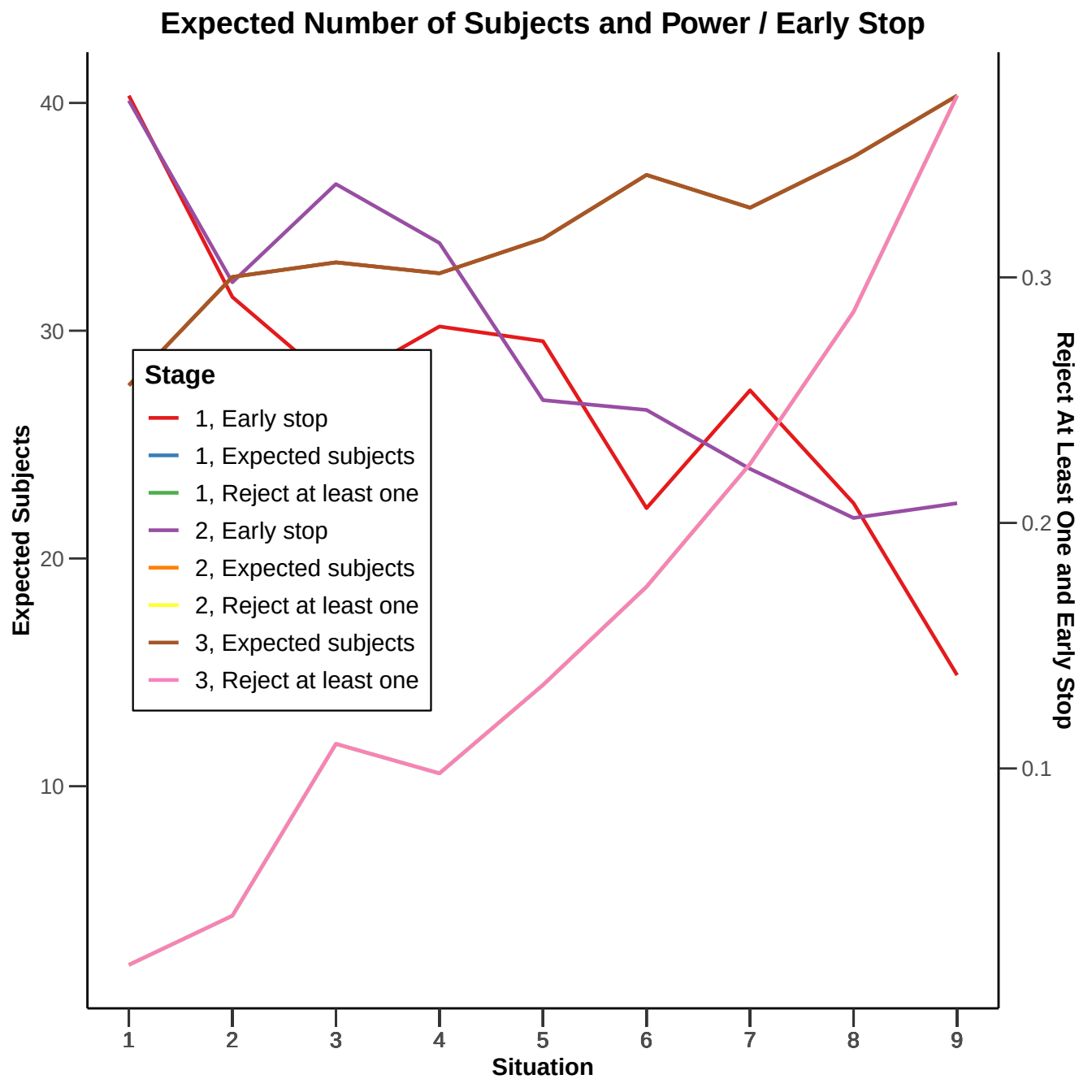

Overall Success
Overall Success
0.3
0.2
0.1
1
2
3
4
5
6
7
8
9
Situation

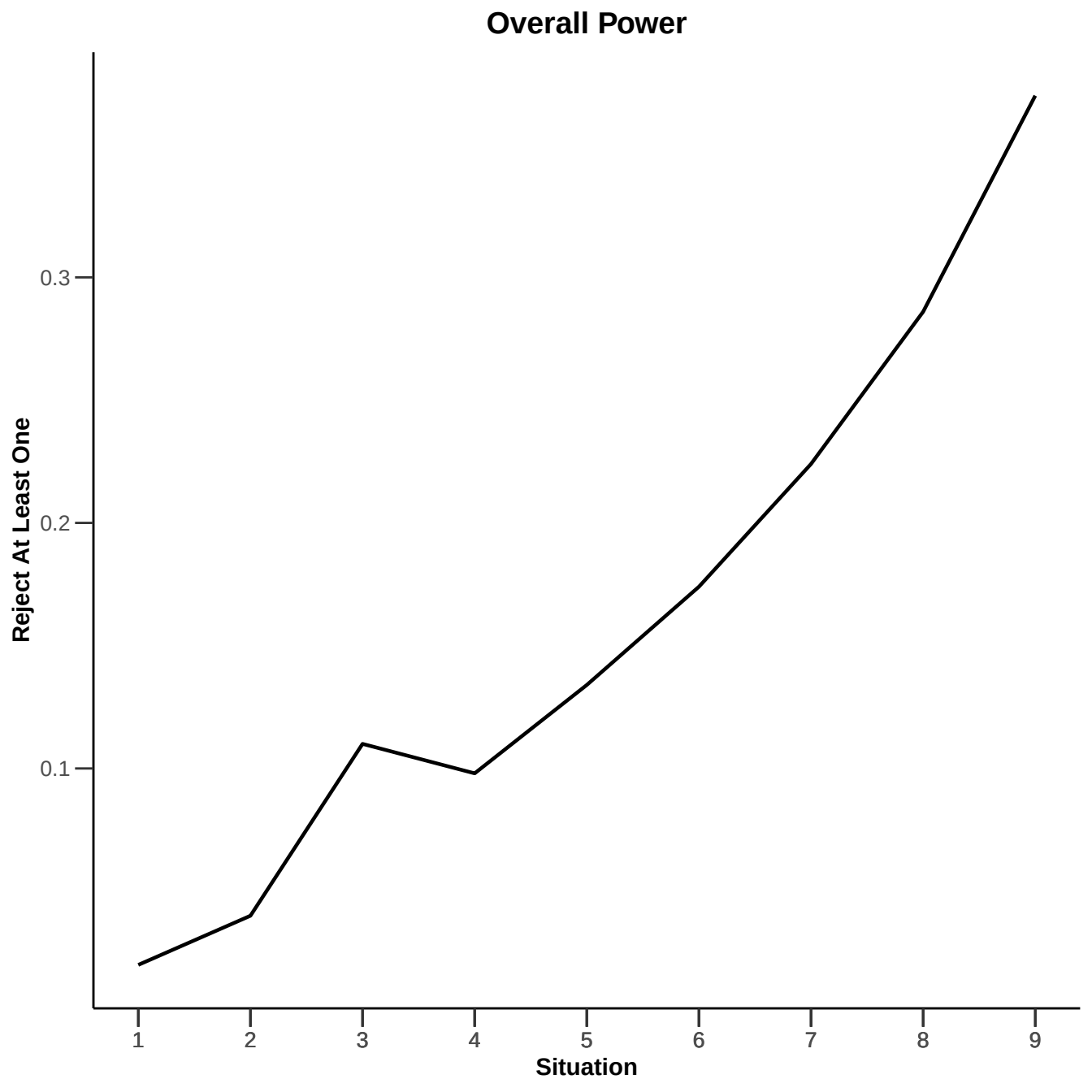

Success per Stage
Stage
1
2
3
0.3
0.2
0.1
0.0
Success
1
2
3
4
5
6
7
8
9
Situation

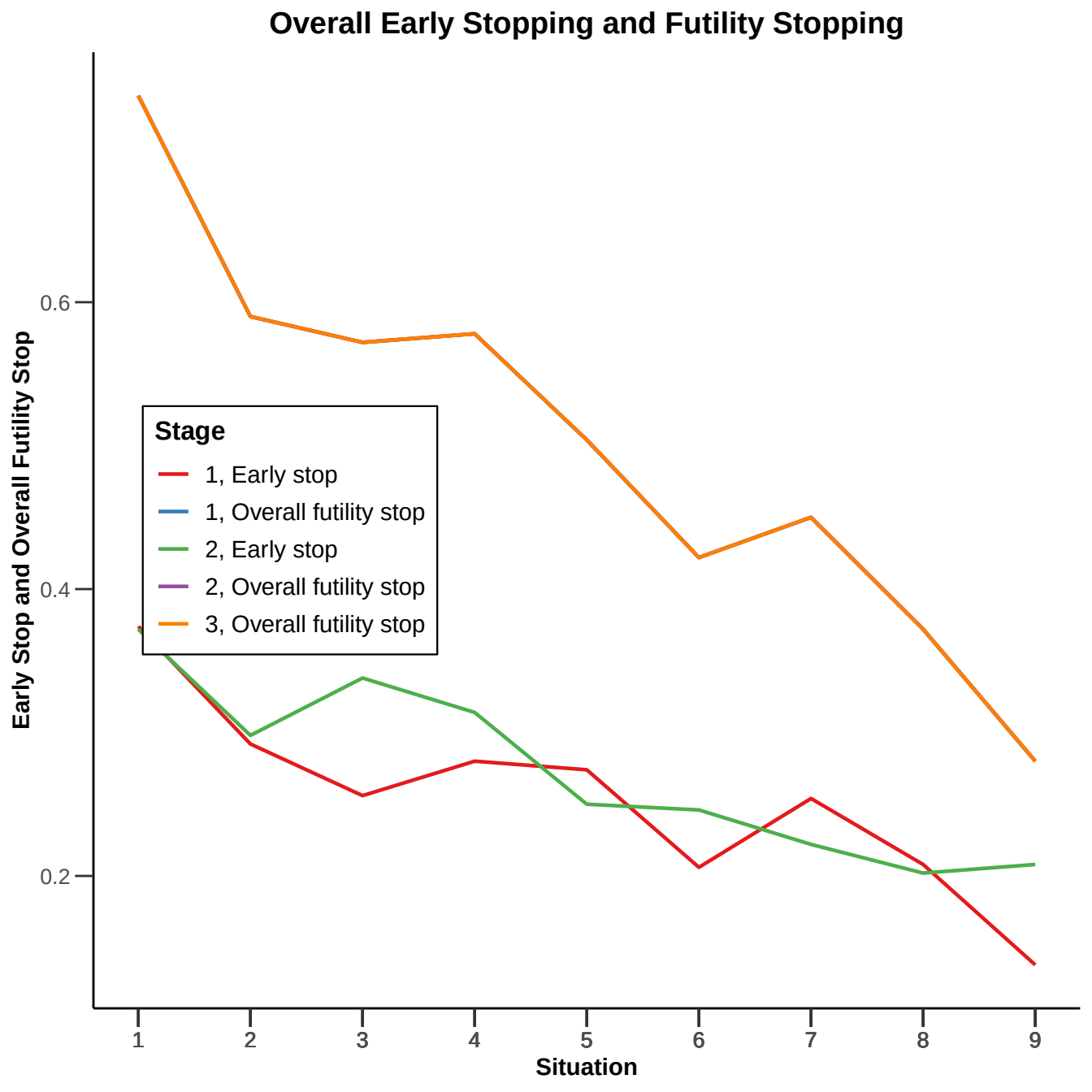

Selected Populations per Stage
Population, Stage
F, 2
F, 3
S1, 2
S1, 3
Selected Populations
0.5
0.4
0.3
0.2
0.1
1
2
3
4
5
6
7
8
9
Situation

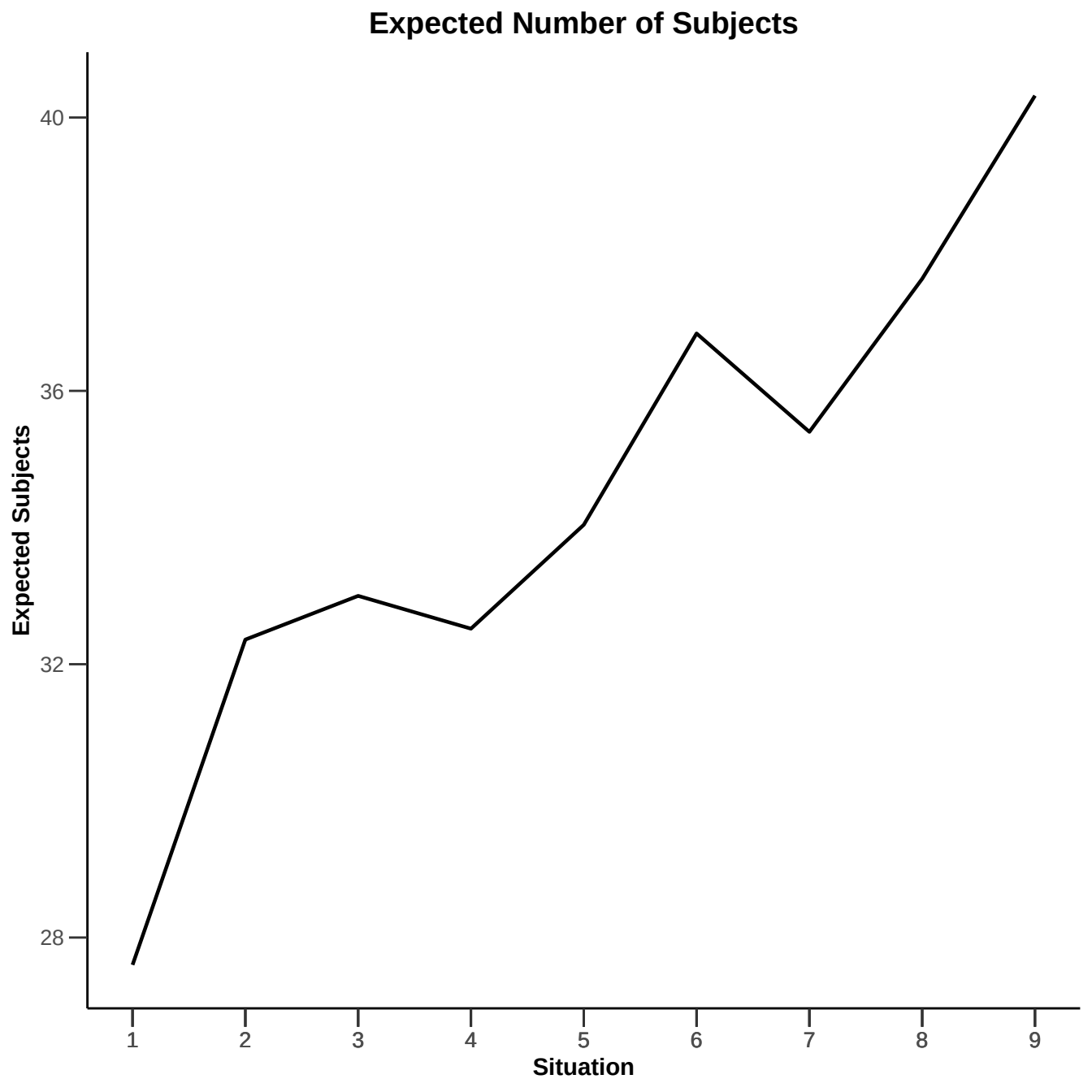

Reject per Stage
Population, Stage
F, 1
F, 2
F, 3
S1, 1
S1, 2
S1, 3
Rejection Probability
0.20
0.15
0.10
0.05
0.00
1
2
3
4
5
6
7
8
9
Situation

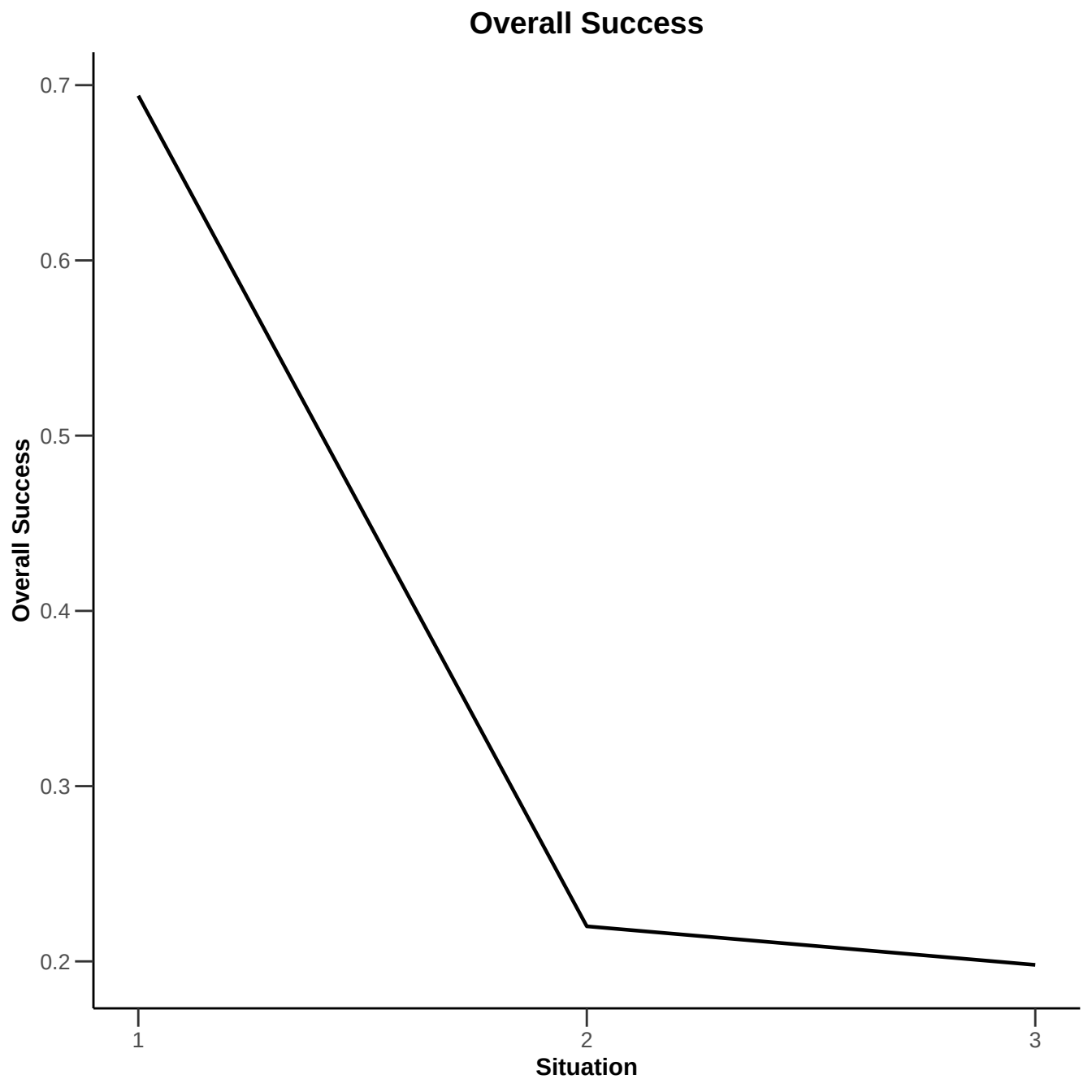

Overall Power and Early Stopping
Early stop, stage 1
Early stop, stage 2
Overall futility stop
Reject at least one
0.6
0.4
0.2
0.0
1
2
3
4
5
6
7
8
9
Situation

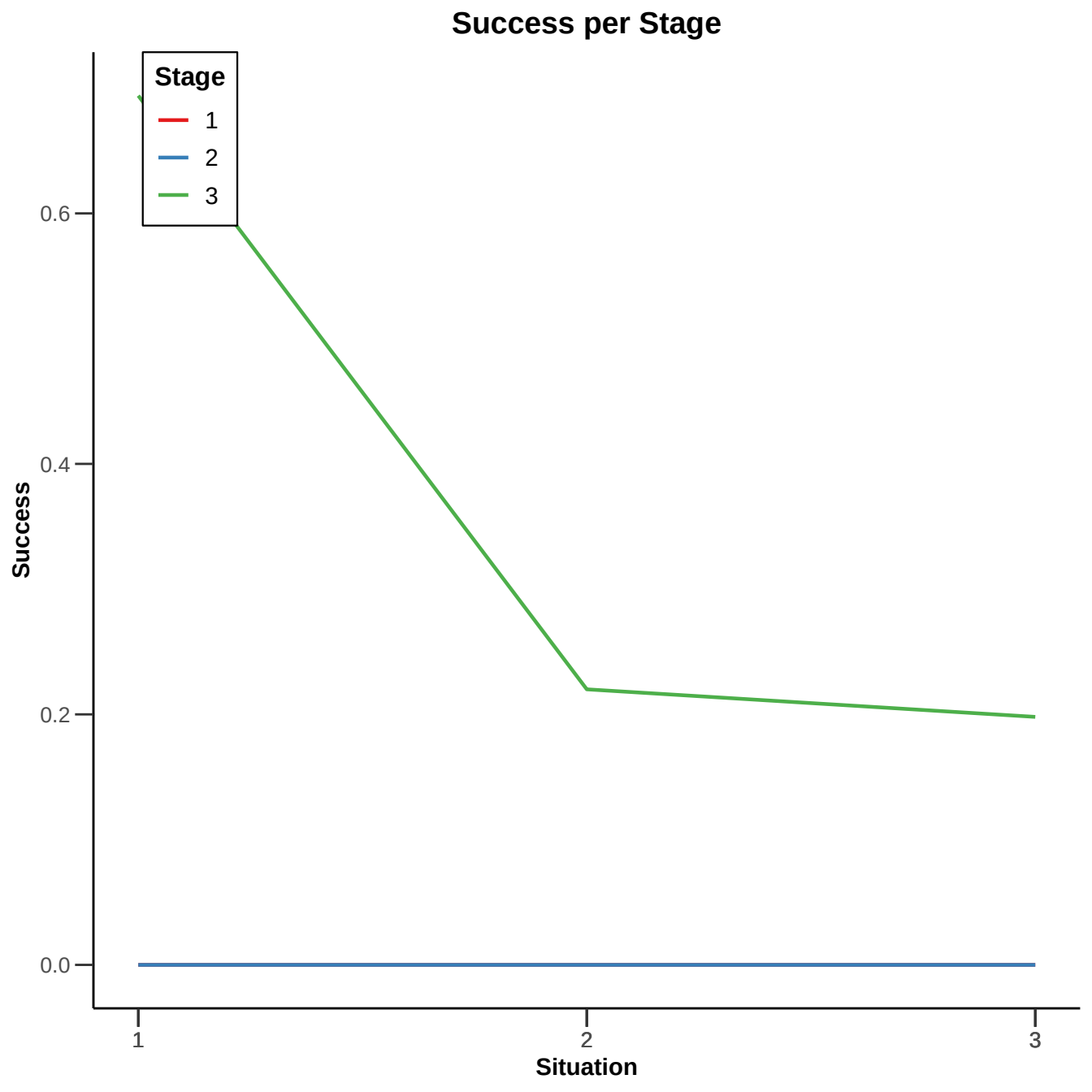

Expected Number of Subjects and Power / Early Stop
Expected Subjects
Reject At Least One and Early Stop
Situation
40
30
20
10
0.3
0.2
0.1
1
2
3
4
5
6
7
8
9
Stage
1, Early stop
1, Expected subjects
1, Reject at least one
2, Early stop
2, Expected subjects
2, Reject at least one
3, Expected subjects
3, Reject at least one

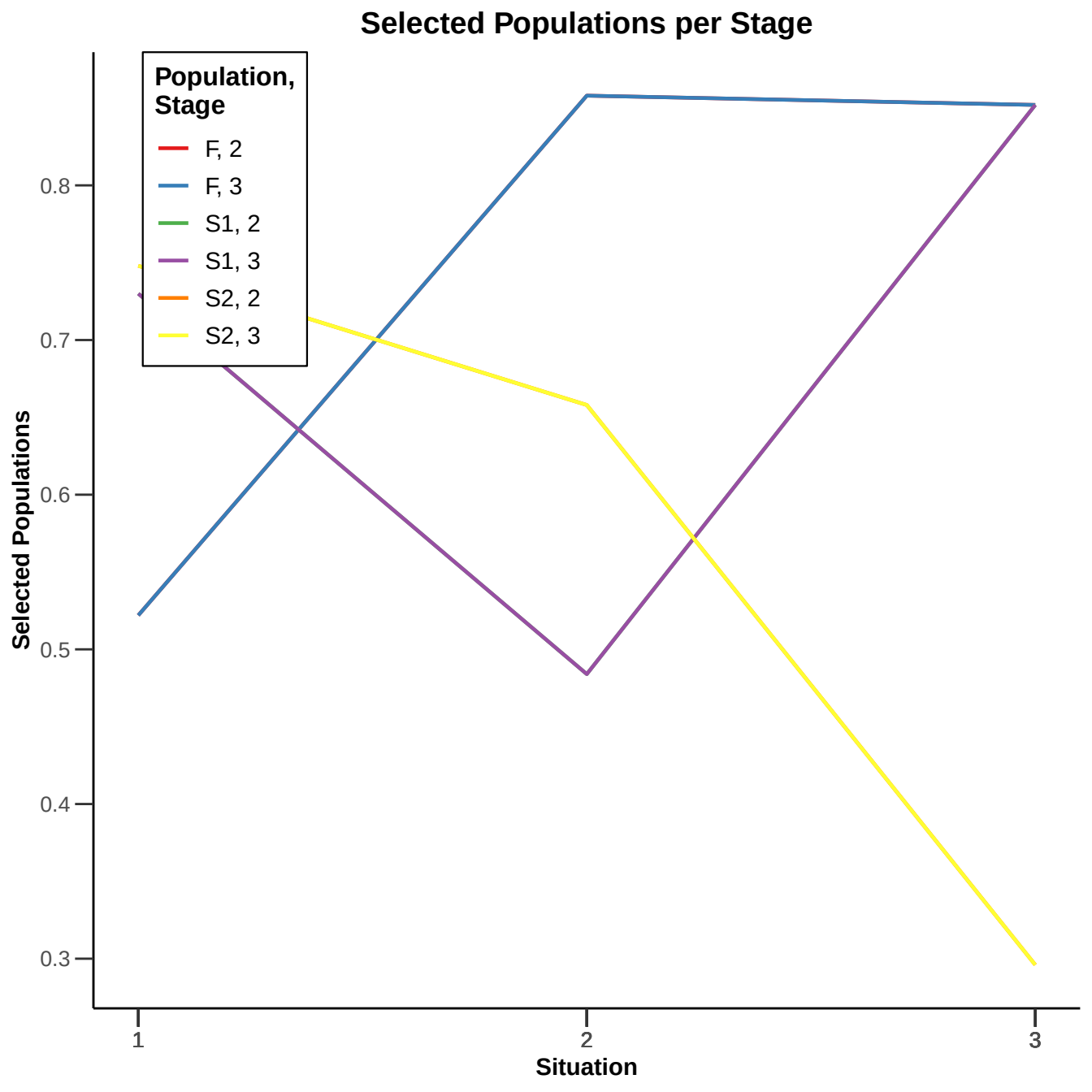

Overall Power
Reject At Least One
0.3
0.2
0.1
1
2
3
4
5
6
7
8
9
Situation

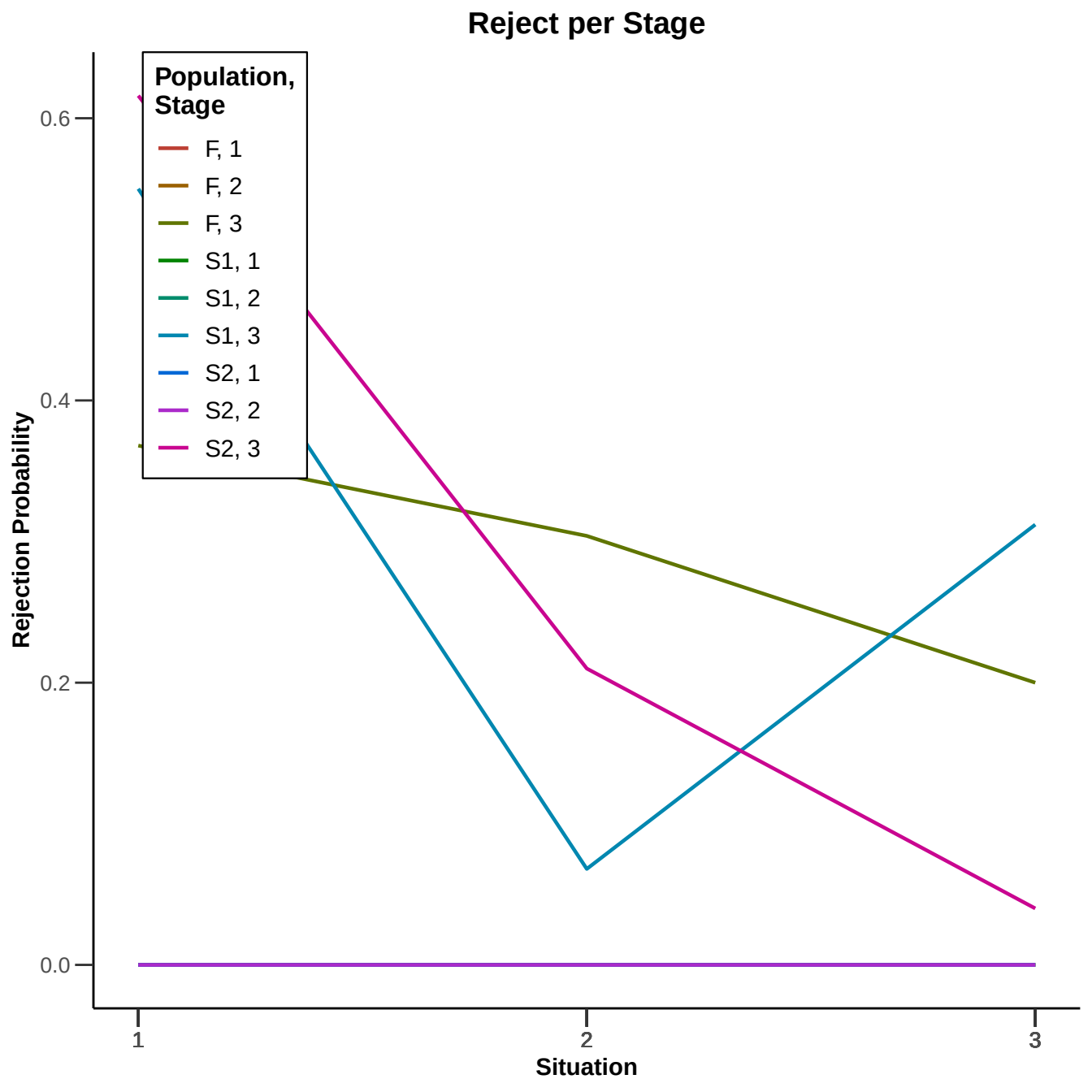

Overall Early Stopping and Futility Stopping
Early Stop and Overall Futility Stop
0.6
0.4
0.2
Stage
1, Early stop
1, Overall futility stop
2, Early stop
2, Overall futility stop
3, Overall futility stop
1
2
3
4
5
6
7
8
9
Situation

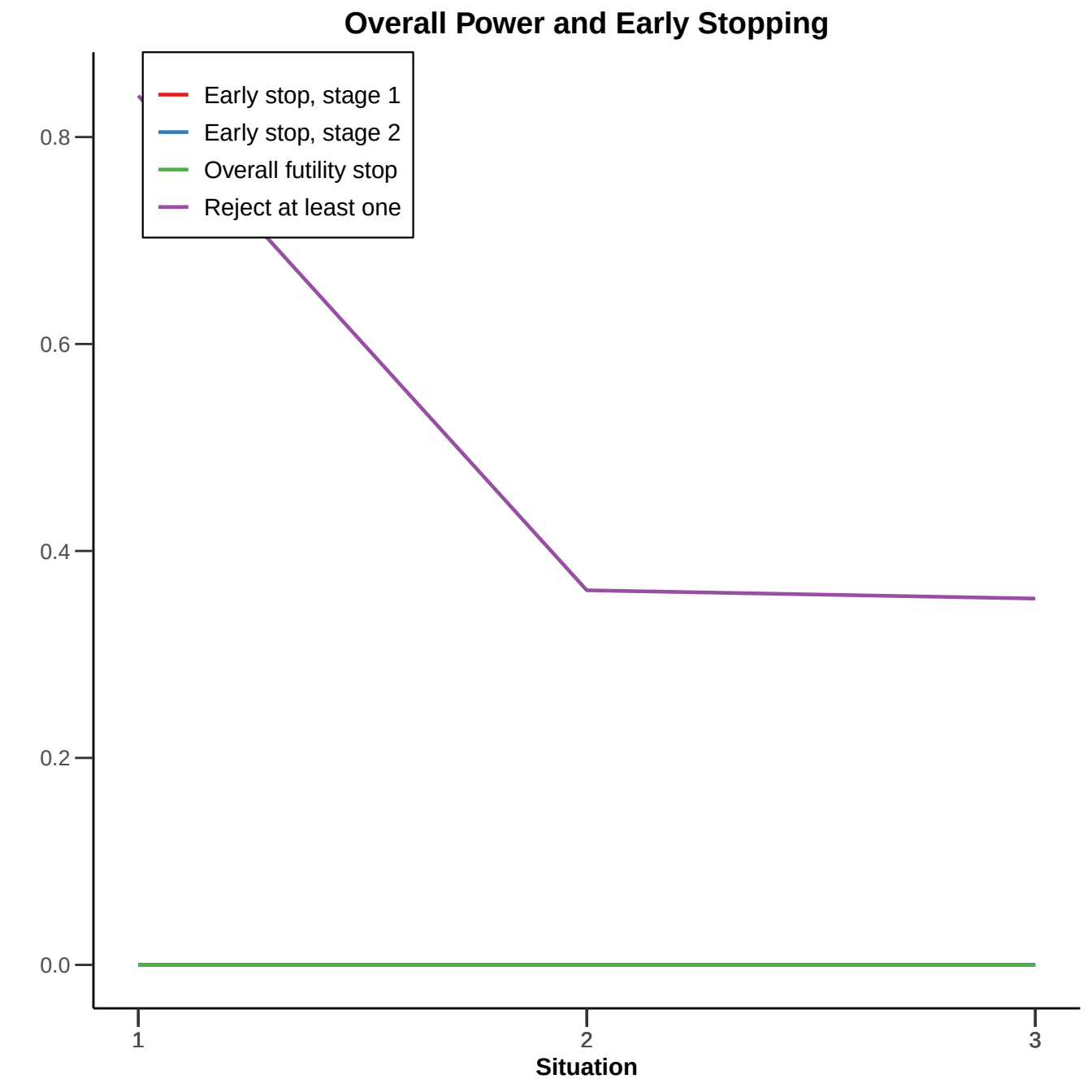

Expected Number of Subjects
40
36
32
28
Expected Subjects
1
2
3
4
5
6
7
8
9
Situation

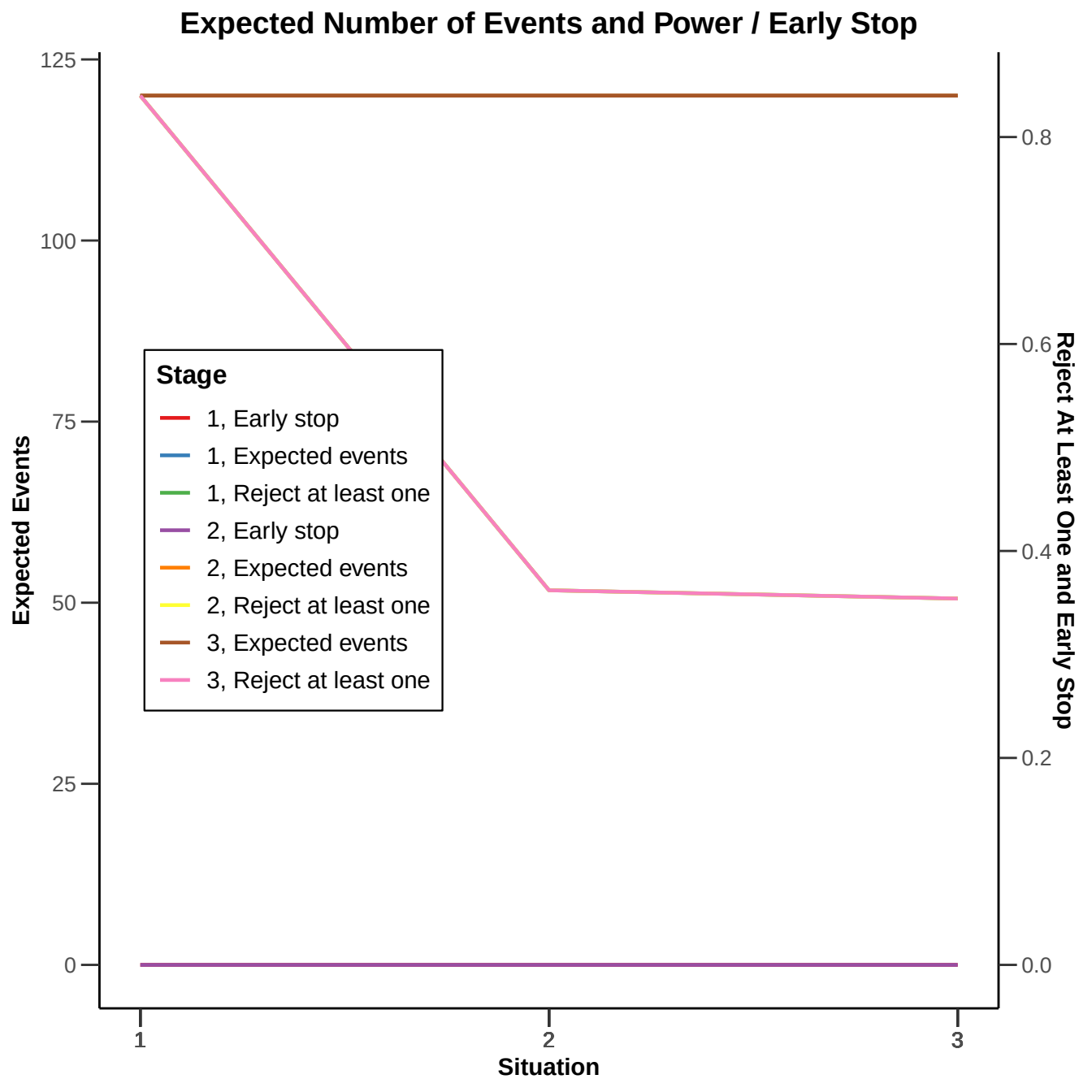

Overall Success
0.7
0.6
0.5
0.4
0.3
0.2
Overall Success
1
2
3
Situation

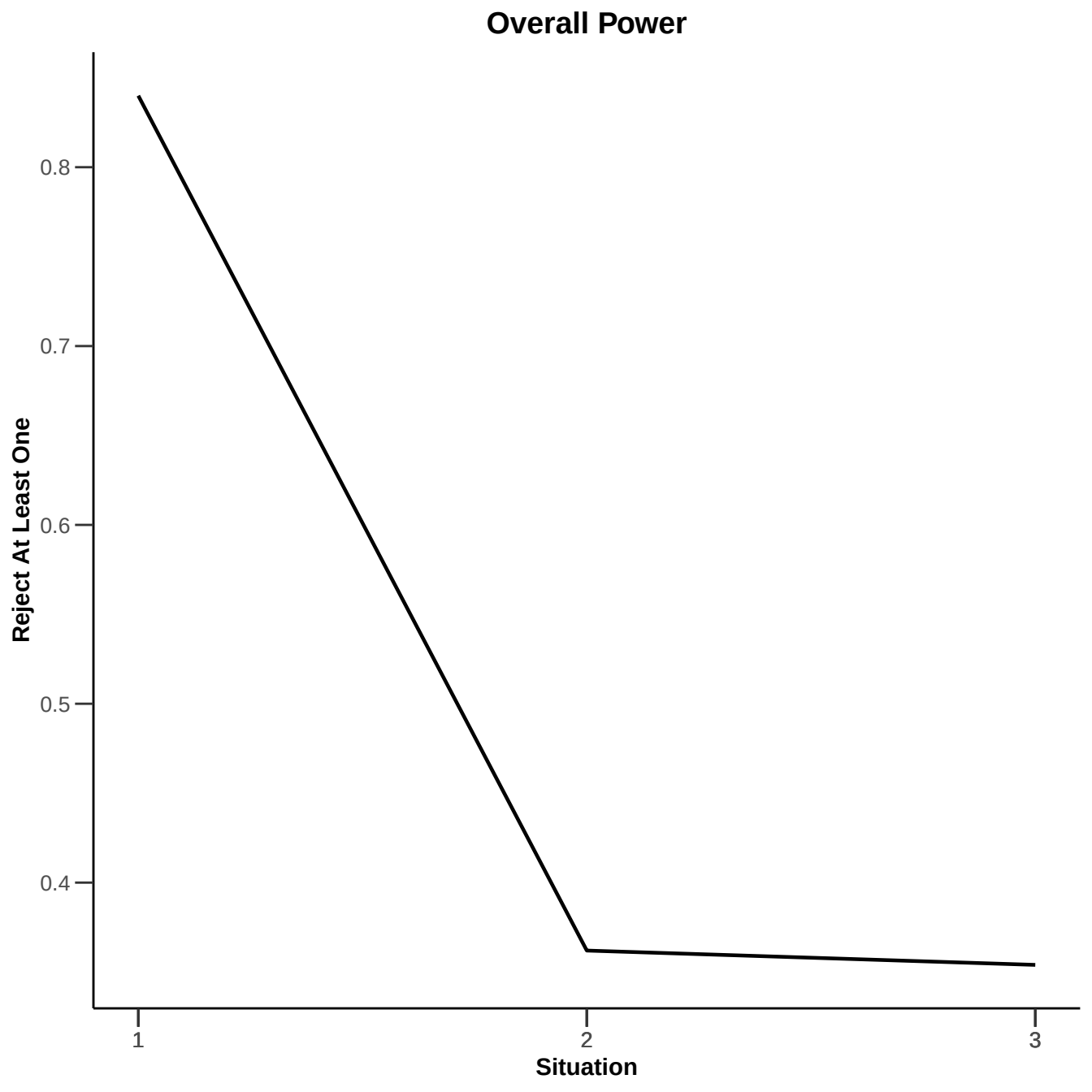

Success per Stage
Stage
1
2
3
0.6
0.4
0.2
0.0
Success
1
2
3
Situation

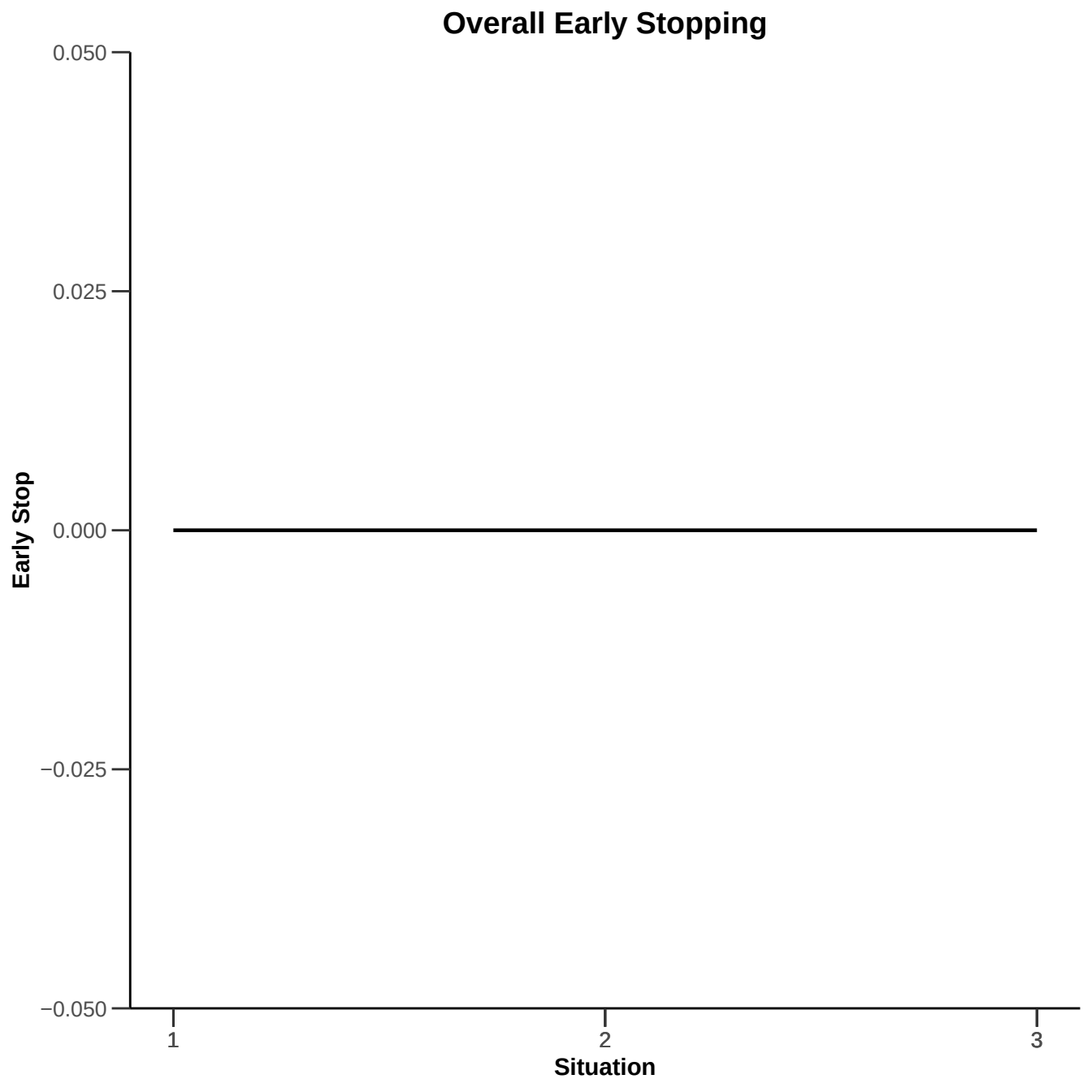

Selected Populations per Stage
Population, Stage
F, 2
F, 3
S1, 2
S1, 3
S2, 2
S2, 3
Selected Populations
0.8
0.7
0.6
0.5
0.4
0.3
1
2
3
Situation

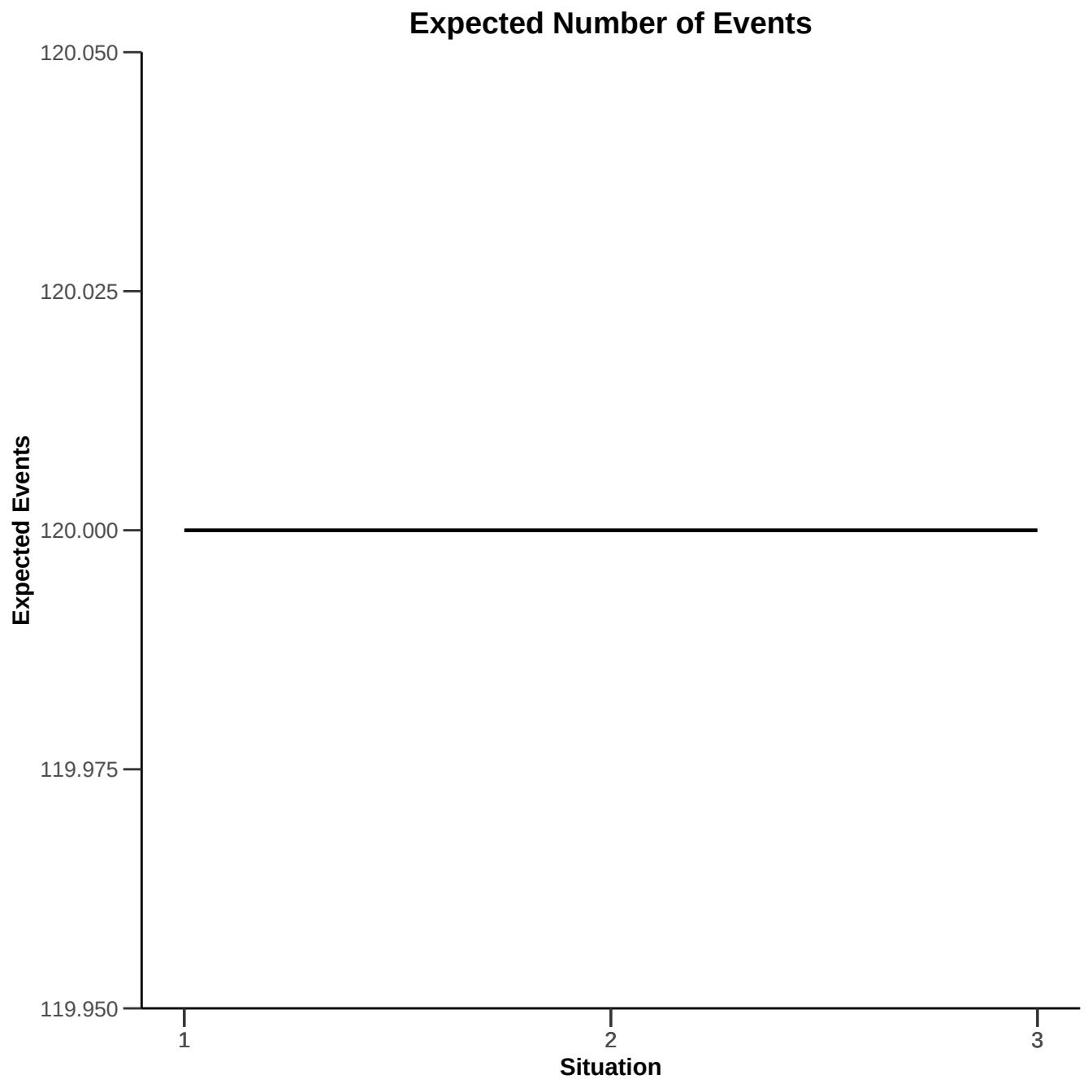

Reject per Stage
Population, Stage
F, 1
F, 2
F, 3
S1, 1
S1, 2
S1, 3
S2, 1
S2, 2
S2, 3
Rejection Probability
0.6
0.4
0.2
0.0
1
2
3
Situation


Overall Power and Early Stopping
Early stop, stage 1
Early stop, stage 2
Overall futility stop
Reject at least one
0.8
0.6
0.4
0.2
0.0
1
2
3
Situation


Expected Number of Events and Power / Early Stop
125
100
75
50
25
0
Expected Events
0.8
0.6
0.4
0.2
0.0
Reject At Least One and Early Stop
Stage
1, Early stop
1, Expected events
1, Reject at least one
2, Early stop
2, Expected events
2, Reject at least one
3, Expected events
3, Reject at least one
1
2
3
Situation


Overall Power
Reject At Least One
0.8
0.7
0.6
0.5
0.4
1
2
3
Situation


Overall Early Stopping
0.050
0.025
0.000
−0.025
−0.050
Early Stop
1
2
3
Situation


Expected Number of Events
120.050
120.025
120.000
119.975
119.950
Expected Events
1
2
3
Situation