**Figure 2 – figure supplement 1.** Standardized mean differences for all 14 single vs multilaboratory comparisons and sub-groups by total quality score

**Study name Time point**

Reimer 1985

**Single vs Multi**

Multi

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

-0.08 -0.70 0.53



**Multi** -0.08 -0.70 0.53

i

Jugdut (a) 1980

Romson (a) 1980

Jugdut (b) 1981

Darsee 1981

Romson (b) 1982

Kirlin 1982

Brown 1983

Flynn 1984

Jugdut (c) 1985

Allan 1985

Single Single Single Single Single Single Single Single Single Single

-1.41 -2.26 -0.55

-2.65 -4.35 -0.95

-1.15 -1.84 -0.45

-1.70 -2.85 -0.55

-1.24 -2.13 -0.35

-0.43 -1.46 0.59

0.92 0.01 1.82

-1.00 -1.68 -0.33

-0.79 -1.47 -0.12

1.28 0.23 2.32

**Single** -0.76 -1.36 -0.16

**-8.00 -4.00**

**0.00 4.00 8.00**

**Favours Treatment Favours Control**

**Study name Time point**

Reimer 1985

**Single vs Multi**

Multi

**Quality Score**

<3

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

-0.08 -0.70 0.53



**Multi OVERALL** -0.08 -0.70 0.53

Jugdut (a) 1980

Romson (a) 1980

Jugdut (b) 1981

Darsee 1981

Romson (b) 1982

Kirlin 1982

Brown 1983

Flynn 1984

Jugdut (c) 1985

Allan 1985

Single <3

Single <3

Single <3

Single <3

Single <3

Single <3

Single <3

Single <3

Single <3

Single <3

-1.41 -2.26 -0.55

-2.65 -4.35 -0.95

-1.15 -1.84 -0.45

-1.70 -2.85 -0.55

-1.24 -2.13 -0.35

-0.43 -1.46 0.59

0.92 0.01 1.82

-1.00 -1.68 -0.33

-0.79 -1.47 -0.12

1.28 0.23 2.32

**Single OVERALL** -0.76 -1.36 -0.16

**-8.00 -4.00**

**0.00 4.00 8.00**

**Favours Treatment Favours Control**

**Study name Time point**

Alam 2009

**Single vs Multi**

Multi

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

2.19 1.25 3.12

**Multi 2.19 1.25 3.12**

Alam 2011

Lee 2013

Schechtman 2019

Sheppard 2018

Sheppard 2019

Single Single Single Single Single

6.75 4.13 9.37

0.58 -0.32 1.47

0.53 -0.10 1.16

1.00 -0.20 2.20

0.69 -0.14 1.51

**Single 1.28 0.25 2.31**

**-8.00 -4.00 0.00 4.00** **8.00**

**Favours Treatment Favours Control**

**Study name Time point**

Alam 2009

**Single vs Multi**

Multi

**Time point**

<3

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

2.19 1.25 3.12

**Multi OVERALL 2.19 1.25 3.12**

Alam 2011

Lee 2013

Schechtman 2019

Sheppard 2018

Sheppard 2019

Single <3

Single <3

Single <3

Single <3

Single <3

6.75 4.13 9.37

0.58 -0.32 1.47

0.53 -0.10 1.16

1.00 -0.20 2.20

0.69 -0.14 1.51

**Single OVERALL 1.28 0.25 2.31**

**-8.00 -4.00 0.00 4.00** **8.00**

**Favours Treatment Favours Control**

**Study name Time point**

Spoerke 2009

**Single vs Multi**

Multi

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

0.56 -0.44 1.56

**Multi 0.56 -0.44 1.56**

Shuja 2008

Shuja 2011

Imam 2013

Halaweish 2016

Georgoff 2017

Single Single Single Single Single

-0.27 -1.41 0.87

-0.65 -1.93 0.62

0.52 -0.74 1.78

-1.31 -2.67 0.06

-0.08 -1.32 1.16

**Single -0.32 -0.89 0.24**

**-4.00**

**-2.00 0.00 2.00 4.00**

**Favours Treatment Favours Control**

**Study name Time point**

Spoerke 2009

**Single vs Multi**

Multi

**Quality Score**

<3

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

0.56 -0.44 1.56

**Multi OVERALL 0.56 -0.44 1.56**

Shuja 2008

Shuja 2011

Imam 2013

Halaweish 2016

Georgoff 2017

Single <3

Single <3

Single <3

Single <3

Single <3

-0.27 -1.41 0.87

-0.65 -1.93 0.62

0.52 -0.74 1.78

-1.31 -2.67 0.06

-0.08 -1.32 1.16

**Single OVERALL -0.32 -0.89 0.24**

**-4.00**

**-2.00 0.00 2.00 4.00**

**Favours Treatment Favours Control**

**Study name Time point**

Jones (i) 2016

Jones (ii) 2016

Jones (iii) 2016

**Single vs Multi**

Multi Multi Multi

**Statistics for each study Std diff in means and 95% CI Std diff Lower Upper**

**in means limit limit**

-2.17 -2.89 -1.44



-2.05 -3.06 -1.04

-0.92 -1.72 -0.11

**Multi -1.70 -2.52 -0.89**

Gao 2000

Hatori 2001

Lange 2006

Boengler 2007

Pagel 2007

Lie 2010

Roesner 2010

Smul 2011

Eckle 2012

YangZ 2013

Single Single Single Single Single Single Single Single Single Single

-2.82 -4.12 -1.51

-2.51 -3.91 -1.11

-3.80 -5.44 -2.16

-2.42 -3.65 -1.19

-6.92 -9.59 -4.24

-3.59 -4.80 -2.39

-1.74 -2.89 -0.59

-4.26 -6.15 -2.36

-12.65 -17.83 -7.46

-3.36 -4.76 -1.95

**Single -3.53 -4.45 -2.60**

**-8.00**

**-4.00**

**0.00 4.00 8.00**

**Favours Treatment Favours Control**

**Study name Time point**

Jones (i) 2016

Jones (ii) 2016

Jones (iii) 2016

**Single vs Multi**

Multi Multi Multi

**Quality Score**

≥ **3**

≥ **3**

≥ **3**

**Statistics for each study Std diff in means and 95% CI Std diff Lower Upper**

**in means limit limit**

-2.17 -2.89 -1.44



-2.05 -3.06 -1.04

-0.92 -1.72 -0.11

**Multi OVERALL -1.70 -2.52 -0.89**

Gao 2000

Lange 2006

Boengler 2007

Pagel 2007

Lie 2010

Roesner 2010

Eckle 2012

YangZ 2013

Single Single Single Single Single Single Single Single

**<3** -2.82 -4.12 -1.51

**<3** -3.80 -5.44 -2.16

**<3** -2.42 -3.65 -1.19

**<3** -6.92 -9.59 -4.24

**<3** -3.59 -4.80 -2.39

**<3** -1.74 -2.89 -0.59

**<3** -12.65 -17.83 -7.46

**<3** -3.36 -4.76 -1.95

**<3 -3.65 -4.78 -2.52**

Hatori 2001

Smul 2011

Single Single

≥ **3** -2.51 -3.91 -1.11

≥ **3** -4.26 -6.15 -2.36

≥ **3 -3.26 -4.96 -1.56**

**Single OVERALL -3.53 -4.45 -2.60**

**-8.00**

**-4.00**

**0.00 4.00 8.00**

**Favours Treatment Favours Control**

# Study name Timepoint

Llovera (a) 2015

Llovera (b) 2015

# Single vs Multi

Multi Multi

# Statistics for each study Std diff in means and 95% CI Std diff Lower Upper

**in means limit limit**

-0.03 -0.42 0.36

-0.60 -1.15 -0.04

# Multi -0.28 -0.83 0.27

Becker 2001

Relton (a) 2001

Relton (b) 2001

Liesz (a) 2011

Liesz (b) 2011

Liesz (c) 2011

Langhauser (a) 2014

Langhauser (b) 2014

Neumann 2015

Drieu (a) 2019

Drieu (b) 2019

Single Single Single Single Single Single Single Single Single Single Single

-1.12 -1.94 -0.30

-1.28 -2.03 -0.53

-0.63 -1.42 0.17

-2.35 -3.49 -1.21

-0.36 -1.24 0.53

-0.63 -1.52 0.27

-0.94 -1.86 -0.02

-0.09 -0.97 0.78

-3.04 -4.22 -1.87

-0.54 -1.76 0.68

-0.19 -1.37 0.99

# Single -0.98 -1.45 -0.51

**-4.00 -2.00 0.00 2.00 4.00**

**Favours Treatment Favours Control**

**Study name Timepoint**

Llovera (a) 2015

Llovera (b) 2015

# Single vs Multi

Multi Multi

# Quality Score

≥ 3

≥ 3

# Statistics for each study Std diff in means and 95% CI Std diff Lower Upper

**in means limit limit**

-0.03 -0.42 0.36

-0.60 -1.15 -0.04

# Multi OVERALL -0.28 -0.83 0.27

Becker 2001

Relton (a) 2001

Relton (b) 2001

Liesz (a) 2011

Liesz (b) 2011

Liesz (c) 2011

Neumann 2015

Drieu (a) 2019

Drieu (b) 2019

Single Single Single Single Single Single Single Single Single

<3 -1.12 -1.94 -0.30

<3 -1.28 -2.03 -0.53

<3 -0.63 -1.42 0.17

<3 -2.35 -3.49 -1.21

<3 -0.36 -1.24 0.53

<3 -0.63 -1.52 0.27

<3 -3.04 -4.22 -1.87

<3 -0.54 -1.76 0.68

<3 -0.19 -1.37 0.99

# <3 -1.06 -1.60 -0.52

Langhauser (a) 2014

Langhauser (b) 2014

Single Single

≥ 3 -0.94 -1.86 -0.02

≥ 3 -0.09 -0.97 0.78

≥ **3 -0.41 -1.42 0.60**

# Single OVERALL -0.98 -1.45 -0.51

**-4.00 -2.00 0.00 2.00 4.00**

**Favours Treatment Favours Control**

**Study**

# Time point

# Single vs. Multi

# Statistics for each study Std diff in means and 95% CI Std diff Lower Upper

**in means limit limit**



Maysami 2015

Multi

-1.45 -1.90 -1.00

# Multi -1.45 -1.90 -1.00

Boutin 2001

Touzani 2002

Mulcachy (a) 2003

Mulcachy (b) 2003

Tsai 2003

Le Feuvre 2003

Craft 2006

Clark 2008

Pradillo (a) 2012

Pradillo (b) 2012

Denes 2014

Girard 2014

Single Single Single Single Single Single Single Single Single Single Single Single

-1.04 -1.91 -0.16

-1.60 -2.73 -0.48

-5.16 -7.51 -2.80

-3.82 -5.26 -2.38

-2.68 -3.89 -1.48

-1.37 -2.54 -0.21

0.27 -0.69 1.23

-1.56 -2.75 -0.36

-2.46 -3.81 -1.12

-1.61 -2.92 -0.31

-0.74 -1.86 0.39

-0.64 -1.72 0.43

**Single -1.69 -2.38 -1.01**

**-8.00 -4.00 0.00 4.00 8.00**

**Favours Treatment Favours Control**

**Study**

**Time point**

**Single vs. Multi**

**Quality Score**

**Statistics for each study Std diff in means and 95% CI Std diff Lower Upper**

**in means limit limit**



Maysami 2015

Multi

≥ 3 -1.45 -1.90 -1.00

# Multi OVERALL -1.45 -1.90 -1.00

Boutin 2001

Touzani 2002

Mulcachy (a) 2003

Mulcachy (b) 2003

Tsai 2003

Le Feuvre 2003

Craft 2006

Clark 2008

Denes 2014

Girard 2014

Single Single Single Single Single Single Single Single Single Single

<3 -1.04 -1.91 -0.16

<3 -1.60 -2.73 -0.48

<3 -5.16 -7.51 -2.80

<3 -3.82 -5.26 -2.38

<3 -2.68 -3.89 -1.48

<3 -1.37 -2.54 -0.21

<3 0.27 -0.69 1.23

<3 -1.56 -2.75 -0.36

<3 -0.74 -1.86 0.39

<3 -0.64 -1.72 0.43

# <3 -1.64 -2.43 -0.85

Pradillo (a) 2012

Pradillo (b) 2012

Single Single

≥ 3 -2.46 -3.81 -1.12

≥ 3 -1.61 -2.92 -0.31

≥ **3 -2.03 -2.96 -1.09**

**Single OVERALL -1.69 -2.38 -1.01**

**-8.00 -4.00 0.00 4.00 8.00**

**Favours Treatment Favours Control**

**Study name Time point**

**Single vs Multi**

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Bramlett (i) | 2016 | Multi | -0.44 | -1.33 | 0.45 |
| Bramlett (ii) | 2016 | Multi | 0.18 | -0.62 | 0.98 |
| Bramlett (iii) | 2016 | Multi | 0.89 | 0.13 | 1.65 |
| **Multi** |  |  | 0.24 | -0.51 | 0.98 |

**Single (Peng SR)** -1.72 -2.36 -1.07

**-8.00 -4.00**

**0.00 4.00 8.00**

**Favours Treatment Favours Control**

**Study name Time point**

**Single vs Multi**

**Quality Score**

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Bramlett (i) | 2016 | Multi | ≥ **3** | -0.44 | -1.33 | 0.45 |
| Bramlett (ii) | 2016 | Multi | ≥ **3** | 0.18 | -0.62 | 0.98 |
| Bramlett (iii) | 2016 | Multi | ≥ **3** | 0.89 | 0.13 | 1.65 |
| **Multi OVERALL** |  |  |  | 0.24 | -0.51 | 0.98 |

**Single (Peng SR) OVERALL**

< **3** -1.72 -2.36 -1.07

**-8.00 -4.00**

**0.00 4.00 8.00**

**Favours Treatment Favours Control**

# Study name Time point

Browning (FPI) 2016

Browning (CCI) 2016

Browning (PBBI) 2016

**Single vs Multi**

Multi Multi Multi

# Statistics for each study Std diff in means and 95% CI

**Std diff Lower Upper in means limit limit**

0.52 -0.31 1.35

-0.60 -1.50 0.30

-0.46 -1.29 0.37

# Multi -0.17 -0.86 0.52

Zou (i) 2013

Zou (ii) 2015

Caudle 2016

Jin 2016

Single Single Single Single

0.07 -0.73 0.87

-1.14 -2.00 -0.27

-0.61 -1.45 0.22

-0.99 -2.02 0.05

# Single -0.63 -1.18 -0.08

**-2.00 -1.00 0.00 1.00 2.00**

**Favours Treatment Favours Control**

# Study name Time point

Browning (FPI) 2016

Browning (CCI) 2016

Browning (PBBI) 2016

**Single vs Multi**

Multi Multi Multi

# Quality Score

≥ 3

≥ 3

# Statistics for each study Std diff in means and 95% CI

**Std diff Lower Upper in means limit limit**

0.52 -0.31 1.35

-0.60 -1.50 0.30

-0.46 -1.29 0.37

# Multi OVERALL -0.17 -0.86 0.52

Caudle 2016

Jin 2016

Single Single

<3 -0.61 -1.45 0.22

<3 -0.99 -2.02 0.05

# <3 -0.76 -1.41 -0.11

Zou (i) 2013

Zou (ii) 2015

Single Single

≥ 3 0.07 -0.73 0.87

≥ 3 -1.14 -2.00 -0.27

# ≥ 3 -0.52 -1.71 0.66

**Single OVERALL -0.63 -1.18 -0.08**

# -2.00 -1.00 0.00 1.00 2.00

**Favours Treatment Favours Control**

**Study name**

**Time point**

**Single vs Multi**

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

Dixon (FPI) 2016

Dixon (CCI) 2016

Dixon (PBBI) 2016

Multi Multi Multi

0.60 -0.28 1.47

0.24 -0.65 1.12

-0.99 -1.75 -0.22

# Multi -0.07 -1.05 0.91

Scheff 1999

Sullivan (i) 2000

Fukui 2003

Gabbita 2005

Mbye 2009

Sullivan (ii) 2011

Vlodavsky 2015

Karlsson 2019

Single Single Single Single Single Single Single Single

-2.90 -4.20 -1.60

-3.59 -5.59 -1.59

-0.50 -1.75 0.76

1.53 0.24 2.81

-2.02 -3.23 -0.82

1.52 0.41 2.63

-3.12 -4.58 -1.66

-1.04 -1.90 -0.19

# Single -1.20 -2.50 0.09

# -8.00 -4.00

**Favours Treatment**

# 0.00 4.00 8.00

**Favours Control**

**Study name**

**Time point**

**Single vs Multi**

**Quality Score**

**Statistics for each study Std diff in means and 95% CI**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | **Std diff in means** | **Lower limit** | **Upper limit** |
| Dixon (FPI) | 2016 | Multi | ≥ 3 | 0.60 | -0.28 | 1.47 |
| Dixon (CCI) | 2016 | Multi | ≥ 3 | 0.24 | -0.65 | 1.12 |
| Dixon (PBBI) | 2016 | Multi | ≥ 3 | -0.99 | -1.75 | -0.22 |
| **Multi OVERALL** |  |  |  | **-0.07** | **-1.05** | **0.91** |
| Scheff | 1999 | Single | <3 | -2.90 | -4.20 | -1.60 |
| Sullivan (i) | 2000 | Single | <3 | -3.59 | -5.59 | -1.59 |
| Fukui | 2003 | Single | <3 | -0.50 | -1.75 | 0.76 |
| Gabbita | 2005 | Single | <3 | 1.53 | 0.24 | 2.81 |
| Mbye | 2009 | Single | <3 | -2.02 | -3.23 | -0.82 |
| Sullivan (ii) | 2011 | Single | <3 | 1.52 | 0.41 | 2.63 |
| **<3** |  |  |  | -0.93 | -2.63 | 0.77 |
| Vlodavsky | 2015 | Single | ≥ 3 | -3.12 | -4.58 | -1.66 |
| Karlsson | 2019 | Single | ≥ 3 | -1.04 | -1.90 | -0.19 |
| ≥ **3** |  |  |  | -1.99 | -4.02 | 0.03 |

**Single OVERALL -1.20 -2.50 0.09**

# -8.00 -4.00

**Favours Treatment**

# 0.00 4.00 8.00

**Favours Control**

# Study name Time point

Gill 2016

# Single vs Multi

Multi

# Statistics for each study Std diff in means and 95% CI

**Std diff Lower Upper in means limit limit**

-0.13 -0.52 0.27

# Multi -0.13 -0.52 0.27

Ablamunitis 2012

Besançon 2018

Single Single

-0.72 -1.30 -0.14

-0.72 -1.38 -0.07

**Single -0.72 -1.16 -0.29**

**-2.00**

**-1.00**

**0.00 1.00 2.00**

**Favours Treatment Favours Control**

**Study name Time point**

Gill 2016

# Single vs Multi

Multi

# Quality Score

<3

# Statistics for each study Std diff in means and 95% CI

**Std diff Lower Upper in means limit limit**

-0.13 -0.52 0.27

# Multi OVERALL -0.13 -0.52 0.27

Ablamunitis 2012

Besançon 2018

Single <3

Single <3

-0.72 -1.30 -0.14

-0.72 -1.38 -0.07

**Single OVERALL -0.72 -1.16 -0.29**

**-2.00**

**-1.00**

**0.00 1.00 2.00**

**Favours Treatment Favours Control**

**Study name Time point**

Mountney (FPI) 2016

Mountney (CCI) 2016

Mountney (PBBI) 2016

# Single vs Multi

Multi Multi Multi

# Statistics for each study Std diff in means and 95% CI

**Std diff Lower Upper in means limit limit**

0.26 -0.64 1.17

0.10 -0.83 1.03

0.18 -0.59 0.95

# Multi 0.18 -0.31 0.68

Lu 2007

Wang 2007

Wu 2008

Abrahamson 2009

Chauhan (i) 2010

Chauhan (ii) 2011

Indraswari 2012

Vonder Haar (i) 2014

Mountney 2016

Single Single Single Single Single Single Single Single Single

0.67 -0.23 1.57

-0.49 -1.16 0.18

0.55 -0.45 1.55

1.19 -0.15 2.54

-0.28 -1.27 0.70

-0.87 -1.89 0.16

-0.43 -1.24 0.38

-0.43 -1.46 0.60

-0.45 -1.44 0.54

# Single -0.13 -0.53 0.27

**-2.00 -1.00 0.00 1.00 2.00**

**Favours Treatment Favours Control**

# Study name Time point

Mountney (FPI) 2016

Mountney (CCI) 2016

Mountney (PBBI) 2016

**Single vs Multi**

Multi Multi Multi

# Quality Score

≥ 3

≥ 3

≥ 3

# Statistics for each study Std diff in means and 95% CI

**Std diff Lower Upper in means limit limit**

0.26 -0.64 1.17

0.10 -0.83 1.03

0.18 -0.59 0.95

# Multi OVERALL 0.18 -0.31 0.68

Lu 2007

Wang 2007

Wu 2008

Abrahamson 2009

Chauhan (i) 2010

Chauhan (ii) 2011

Mountney 2016

Single Single Single Single Single Single Single

<3 0.67 -0.23 1.57

<3 -0.49 -1.16 0.18

<3 0.55 -0.45 1.55

<3 1.19 -0.15 2.54

<3 -0.28 -1.27 0.70

<3 -0.87 -1.89 0.16

<3 -0.45 -1.44 0.54

# <3 -0.02 -0.53 0.49

Indraswari 2012

Vonder Haar (i) 2014

Single Single

≥ 3 -0.43 -1.24 0.38

≥ 3 -0.43 -1.46 0.60

# ≥ 3 -0.43 -1.06 0.21

# Single OVERALL -0.13 -0.53 0.27

# -2.00 -1.00 0.00 1.00 2.00

**Favours Treatment Favours Contro**

# Study name Time point

Shear (FPI) 2016

Shear (CCI) 2016

Shear (PBBI) 2016

**Single vs Multi**

Multi Multi Multi

# Statistics for each study Std diff in means and 95% CI

**Std diff Lower Upper in means limit limit**

-0.36 -1.24 0.52

-0.73 -1.54 0.08

-0.25 -0.97 0.47

# Multi -0.43 -0.89 0.03

Hoane (i) 2003

Hoane (ii) 2006

Hoane (iii) 2008

Quigley 2009

Goffus 2010

Swan 2011

Vondar Haar (ii) 2011

Peterson (i) 2012

Vondar Haar (iii) 2014

Peterson (ii) 2015

Single Single Single Single Single Single Single Single Single Single

-1.24 -2.25 -0.23

0.25 -0.41 0.90

-1.64 -2.77 -0.50

-0.14 -1.12 0.84

-0.99 -2.03 0.05

-0.30 -1.36 0.77

-1.31 -2.30 -0.32

-0.98 -1.96 -0.00

0.19 -0.71 1.10

-1.01 -2.21 0.19

# Single -0.65 -1.10 -0.21

**-4.00 -2.00 0.00 2.00 4.00**

**Favours Treatment Favours Control**

# Study name Time point

Shear (FPI) 2016

Shear (CCI) 2016

Shear (PBBI) 2016

**Single vs Multi**

Multi Multi Multi

# Quality Score

≥ 3

≥ 3

≥ 3

# Statistics for each study Std diff in means and 95% CI

**Std diff Lower Upper in means limit limit**

-0.36 -1.24 0.52

-0.73 -1.54 0.08

-0.25 -0.97 0.47

# Multi OVERALL -0.43 -0.89 0.03

Hoane (i) 2003

Hoane (ii) 2006

Hoane (iii) 2008

Quigley 2009

Vondar Haar (ii) 2011

Single Single Single Single Single

<3 -1.24 -2.25 -0.23

<3 0.25 -0.41 0.90

<3 -1.64 -2.77 -0.50

<3 -0.14 -1.12 0.84

<3 -1.31 -2.30 -0.32

**<3** -0.76 -1.54 0.03

Goffus 2010

Swan 2011

Peterson (i) 2012

Vondar Haar (iii) 2014

Peterson (ii) 2015

Single Single Single Single Single

≥ 3 -0.99 -2.03 0.05

≥ 3 -0.30 -1.36 0.77

≥ 3 -0.98 -1.96 -0.00

≥ 3 0.19 -0.71 1.10

≥ 3 -1.01 -2.21 0.19

≥ **3** -0.57 -1.07 -0.06

# Single OVERALL -0.65 -1.10 -0.21

# -4.00 -2.00 0.00 2.00 4.00

**Favours Treatment Favours Control**

**Study name Time point**

Arroyo-Araujo 2019

**Single vs Multi**

Multi

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

-1.15 -1.65 -0.65

**Multi -1.15 -1.65 -0.65**

Silverman (i) 2010

Burket 2011

Mehta 2011

Silverman (ii) 2012

Aguilar-Valles 2015

Modi 2018

Single Single Single Single Single Single

-1.73 -2.74 -0.73

2.15 1.05 3.25

-1.13 -1.99 -0.26

-1.24 -2.15 -0.33

-2.03 -3.02 -1.04

-0.96 -1.89 -0.04

**Single -0.84 -1.92 0.24**

**-4.00**

**-2.00 0.00**

**2.00 4.00**

**Favours Treatment Favours Control**

**Study name Time point**

Arroyo-Araujo 2019

**Single vs Multi**

Multi

**Quality Score**

≥ 3

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

-1.15 -1.65 -0.65

**Multi OVERALL -1.15 -1.65 -0.65**

Burket 2011

Mehta 2011

Silverman 2012

Aguilar-Valles 2015

Modi 2018

Single <3

Single <3

Single <3

Single <3

Single <3

2.15 1.05 3.25

-1.13 -1.99 -0.26

-1.24 -2.15 -0.33

-2.03 -3.02 -1.04

-0.96 -1.89 -0.04

**<3 -0.66 -1.92 0.60**

Silverman 2010

Single ≥ 3

-1.73 -2.74 -0.73

≥ 3 -1.73 -2.74 -0.73

[Single OVERALL -0.84 -1.92 0.24](#_TOC_250002)

-4.00

[-2.00 0.00](#_TOC_250001)

[2.00 4.00](#_TOC_250000)

**Favours Treatment Favours Control**

**Study name Time point**

Jha (CCI) 2020

Jha (PBBI) 2020

Jha (FPI) 2020

**Single vs Multi**

Multi Multi Multi

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

-0.03 -0.75 0.69

-1.02 -1.96 -0.09

-0.06 -0.86 0.74

**Multi -0.31 -0.91 0.28**

Simard 2009

Zweckberger 2014

Xu 2017

Jha 2019

Gerzanich 2019

Single Single Single Single Single

-1.05 -1.98 -0.11

-2.81 -4.04 -1.57

-1.35 -2.73 0.02

-0.11 -1.04 0.81

-2.06 -3.21 -0.92

**Single -1.42 -2.35 -0.50**

**-4.00 -2.00 0.00 2.00** **4.00**

**Favours Treatment Favours Control**

**Study name Time point**

Jha (CCI) 2020

Jha (PBBI) 2020

Jha (FPI) 2020

**Single vs Multi**

Multi Multi Multi

**Quality Score**

≥ 3

≥ 3

≥ 3

**Statistics for each study Std diff in means and 95% CI**

**Std diff Lower Upper in means limit limit**

-0.03 -0.75 0.69

-1.02 -1.96 -0.09

-0.06 -0.86 0.74

**Multi OVERALL -0.31 -0.91 0.28**

Simard 2009

Xu 2017

Gerzanich 2019

Single Single Single

<3 -1.05 -1.98 -0.11

<3 -1.35 -2.73 0.02

<3 -2.06 -3.21 -0.92

**<3 -1.43 -2.07 -0.79**

Zweckberger 2014

Jha 2019

Single Single

≥ 3 -2.81 -4.04 -1.57

≥ 3 -0.11 -1.04 0.81

≥ **3 -1.43 -4.07 1.21**

**Single OVERALL -1.42 -2.35 -0.50**

**-4.00 -2.00 0.00 2.00** **4.00**

**Favours Treatment Favours Control**