DIPLOMARBEIT

„Animal studies on digit ratio (2D:4D) as a hormone marker: Systematic review and meta-analyses“

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1. Introduction

1.1. Historical background

The ratio of the length of the second digit (2D) to the length of the fourth digit (4D), the 2D:4D ratio, is known to be sexually dimorphic. This subtle difference in human hand anatomy has already been known since the late 19th century, resulting from a long established observation that men tend to have longer ring fingers relatively to their second fingers and women tend to have longer second fingers relatively to their ring fingers (Ecker, 1875; Baker, 1888; Weissenberg, 1895).

This sex difference has been brought up again by Manning, Scutt, Wilson & Lewis-Jones in 1998. They suggested that the 2D:4D ratio may be a putative indirect marker of prenatal influence of androgens on the differentiation of digits and gonads and that this differentiation may be under control of the homeobox genes (Hox genes).

Moreover, Manning hypothesized that 2D:4D as a sexual dimorphic trait strikes all pentadactyl tetrapods (Manning, 2002). He suggested that the remodeling limbs of tetrapods, when moving out of aquatic environments about 300 million years ago, simultaneously evolved when gonadal system as well had to adapt to terrestrial life. Possibly these adaptations led to a common underlying genetic mechanism involving the same HOX genes (Zakany, Formental-Ramian, Warot & Duboule, 1997). HOX genes are known to be highly phylogenetically conserved across taxa and to be regulated by sex hormones. The regulatory effects of the endocrine system are able to affect the expression of genes encoding the development of bone components and soft tissues in limb buds (Daftary and Taylor, 2006; Zheng and Cohn, 2011).

1.2. Role of animal models for digit ratio research

Today we understand the essential role of the effects of prenatal androgen exposure on the sexual differentiation of the fetus. There are also profound masculinizing effects on the central nervous system and peripheral tissues (Cohen-Bendahan, van de Beek & Berenbaum, 2005; Hines, 2009). Corresponding with this "organizational" effects of prenatal sex hormones, a multitude of behavioral, cognitive and health-related factors are examined in a large variety of studies (Cohen-Bendahan et al., 2005; Voracek & Loibl, 2009; Voracek, 2011).

It is not possible to directly measure or even manipulate prenatal androgen levels in human fetuses in order to resolve the details of the hormonal mechanisms because of ethical reasons on the one hand and on the other hand, this approach is impaired by the slow course of human development (Breedlove, 2010).

Thus, it is important for research progress in this field to find simple and widely-available methods for examining hormonal effects on human behavior through indirect, non-invasive somatic markers of prenatal sex-hormonal milieu (Hines, 2009). Digit ratio is one such intensely studied prenatal androgen marker, precisely the 2D:4D ratio. In fact, other ratios have been examined as well, and results suggest a good reliability of some of the other digit ratios too, as will be demonstrated in this review.

The investigation of digit ratios on nonhuman animals provides new possibilities for 2D:4D research. It allows experimental study designs, examination of quantitative genetics accounting for digit ratio differences and conclusions about the evolutionary relevance and development of this trait.

1.3. Current state of research

Different species of different taxa have been studied for sex differences in digit ratios as well as for associations between digit ratios and androgen levels and/or behavioral traits: rodents, amphibians, reptiles, birds and nonhuman primates. The growing body of research on digit ratio indicates that this trait generalizes across taxa, but there is substantial variability of outcomes.

Humans and non-human mammals show females to have a higher digit ratio and males to have a lower digit ratio: for laboratory mice see Brown, Finn & Breedlove, 2002; Manning and Bundred, 2003; Yan, Malisch, Hannon, Hurd & Garland, 2008 and Zheng and Cohn, 2011. For rats see McMechan, O'Leary-Moore, Morrison & Hannigan, 2004 and Auger, Le Denmat, Berges. Doridot, Salmon, Canivenc-Lavier & Eustache, 2013. For wood mice see Leoni, Canova & Saino, 2005. For non-human primates see McFadden and Bracht, 2003; McIntyre, Herrmann, Wobber, Halbwax, Mohamba, de Sousa, Atenicia, Cox & Hare, 2009 and Nelson and Shultz, 2010.

On the contrary, reptiles and birds exhibit the opposite pattern of sexual dimorphism with males having a higher ratio than females: for zebra finches see Burley and Foster, 2003. For house sparrows see Navarro, de Lope & Møller, 2007. For hooded crows see Leoni, Rubolini, Romano, Giancamillo & Saino, 2008. For wall lizards see Rubolini, Pupin, Sacchi, Gentilli, Zuffi, Galeotti & Saino, 2006. For green anoles see Chang, Doughty, Wade & Lovern, 2006 and Chang, 2008. For three species of iguanian lizards see Gomes and Kohlsdorf, 2011. For two species of lacertid lizards see Van Damme, Wijnrocx, Boeye, Huyghe & Van Dongen, 2015.

On the other hand, there is conflicting data: some studies found opposite patterns from those described above: for baboons see Roney, Whitham, Leoni, Bellem, Wielebnowski & Mastreipieri, 2004. For mice see Hurd, Bailey, Gongal, Yan, Greer & Pagliardini, 2007. For tree skinks see Rubolini, Pupin, Sacchi, Gentilli, Zuffi, Galeotti & Saino, 2006. For the Australian painted dragon see Tobler, Healey & Olsson, 2011. For three species of newts see Kaczmarski, Kubicka, Tryjanowski & Hromada, 2015. For fire salamander see Balogová, Nelson, Uhrin, Figurová, Ledecký & Zyśk, 2015.

There are also studies that did not find any sexual dimorphism of digit ratios: for mice see Bailey and Hurd, 2004; Manno, 2008 and Yan, Bunning, Wahlsten, & Hurd, 2009. For field voles see Lilley, Laaksonen, Huitu, & Helle, 2009. For Wistar rats see Talarovicová, Krsková, & Blazeková, 2009. For North American red squirrels see Gooderham, 2012 and for rock squirrels see Zhao, Chen, & Li, 2014. For rhesus macaques see Abbott, Colman, Tiefenthaler, Dumesic, & Abbott, 2012. For ring-necked pheasants see Romano, Rubolini, Martinelli, Bonisoli Alquati, & Saino, 2005. For zebra finches see Forstmeier, 2005; Forstmeier, Mueller, & Kempenaers, 2010 and Bogdan, 2009. For barn swallows see Dreiss, Navarro, de Lope, & Moller, 2007; for house sparrows and tree sparrows see Lombardo, Thorpe, Brown, & Sian, 2008. For Balearic sheawaters see Genovart, Louzao, Igual, & Oro, 2008. And for the pied flycatcher see Ruuskanen, Helle, Ahola, Adamczyck, Möstl & Laaksonen, 2011.

1.3.1. Evidence from experimental research

Strong evidence that digit ratio is associated with prenatal androgen and estrogen levels comes from experimental studies. In rodents (rats) a decreased influence of perinatal testosterone through prenatal exposure to alcohol results in lower 2D:3D ratios on both forepaws (McMechen et al. 2004). This difference is due to the higher-alcohol-dose group having a significantly shorter 2D on both forepaws than the control group.

Enhancement of testosterone during pregnancy reduced 2D:4D ratio in male and female Wistar rats (Talarovičová, Kršková & Blažeková, 2009) as a result of shortened second digits and elongated fourth digits relatively to controls.

Zengh and Cohn established the developmental basis of the sexually dimorphic trait of 2D:4D in 2011. They investigated the molecular mechanisms of dimorphism of digit ratio and found out that the developmental mechanism underlying is the balance of androgen to estrogen levels during a narrow window of digit development. They pointed out that the activity of androgen receptors (AR) and estrogen receptors α (ER-α) is higher in 4D than in 2D. Thus inactivation of AR decreases growth of the fourth digit and causes a higher 2D:4D ratio, whereas inactivation of ER-α increases growth of the fourth digit and results in a lower 2D:4D ratio. They also demonstrated that administration of androgen has similar effects as inactivation of ER-α and correspondently an inactivation of AR can be achieved by administration of estrogen. They reasoned that sex hormones differentially regulate the network of genes that control chondrocyte proliferation, leading to differential growth of second and fourth digits in male and female fetuses.

Forstmeier et al. found out that a polymorphism in the ER-α gene explains 11.3% of the variation in digit ratio, whereas no impact of polymorphism was found in the androgen receptor gene (2010).

Auger and colleagues investigated the effects on male Wistar rats exposed to antiandrogenic/estrogenic compounds (bisphenol A, genistein and vinclozolin) during gestation. The results point towards a feminization of digit ratios in male rats through permanently disrupted digit ratio because of endocrine-active substances (Auger, Le Denmat,, Berges, Doridot, Salmon, Canivenc-Lavier & Eustache, 2013). The studies of Talarovičová et al., 2009 as well as Auger et al. 2013 are consistent with the findings of Zeng and Cohn.

McMechan et al. found changes in 2D:3D being lower after prenatal alcohol exposure. They reported the second digit being shorter relatively to controls, whereas no change in length of the fourth digit was detected. The study of McMechan et al. profoundly based on the idea of decreased influence of testosterone because of alcohol. Actually, alcohol is known to have serious effects on limb differentiation, which are mostly a result of mispatterning of the antero-posterior-axis. The same limb defects are caused by a retinoic acid (RA) deficiency. RA is fundamentally involved in gene expression. Metabolism of ethanol depends on the enzymes alcohol dehydrogenase and aldehyde dehydrogenase (ALDH). The same enzymes are needed for the synthesis of retinoic acid. The mechanism, by which alcohol functions to cause limb malformations, is explained by the competition for ALDH. Competition for ALDH ultimately leads to reduced levels of RA (Johnson, Zucker, Hunter & Sulik, 2007).

Since, it cannot be cleared out to which extent alcohol decreases testosterone influence or to which extend the mechanisms explained by Johnson et al. (2007) are responsible for changes in limbs in the study of McMechan et al. (2004), the results cannot be well interpreted.

In birds, Romano and colleagues used testosterone injection into pheasant eggs to examine effects on digit ratio. Although they found no general sex dimorphism of this trait at all, they observed a higher 2D:3D ratio for females under experimental condition, but not for males (Romano, Rubolini, Martinelli, Alquati, Saino, 2005). In birds, the digit ratio is commonly known to show the opposite pattern than in mammals: that is, digit ratio being relatively smaller for females than males. Hence, the results are consistent with the basic principle of female birds having a lower ratio than males. Saino et al. used injection of estradiol into pheasant eggs to investigate the outcome for digit ratio. What they found were general sexual differences for some digit ratios on the right foot and furthermore, they detected a feminized 2D:4D ratio on the right foot of males, being lower than in controls, which is also consistent with the expected outcome (Saini, Rubolini, Romano & Boncoraglio, 2007).

In contrast, Forstmeier used estradiol injection into eggs of zebra finches and found no effect on nestlings' 2D:4D ratio (Forstmeier, Rochester & Millam, 2008).

Tobler et al. found sex differences in the Australian painted dragon, being smaller for males – contradictory to the common pattern of smaller ratios in females for these taxa. In addition, they conducted experimental elevation of yolk testosterone and detected significantly increased 3D:4D in hatchlings, what is contradictory to the expected outcome (2011).

Abbott and colleagues performed an experimental study on rhesus macaques, the first to use a non-human primate (Abbott, Colman, Tiefenthaler, Dumesic & Abbott, 2012). They exposed dam monkeys to fetal male-typical testosterone levels by subcutaneous injection at different points in time during gestation. The administration of testosterone at early-to-mid gestation resulted in an increased 2D:4D ratio on the right hand. This outcome stands in contrast to the prediction, that testosterone enhancement leads to a more masculinized digit ratio. Instead, the digit ratio shows a hyperfeminine increase in right hands' digit ratio of about 8%, resulting from an elongation of the second finger relatively to controls of about 7% (Abbott et al., 2012).

Against the background of the findings of Abbott et al., the results of McMechan et al. seem more consistent. Whereas testosterone enhancement in the study of Abbott et al. leads to elongation of the second digit, the decreased testosterone influence as a consequence of alcohol exposure in the study of McMechan et al. results in a shorter second digit (McMechan et al. 2004).

An overview of the results from experimentation emphasizes the complexity of developmental pattern and interspecies comparisons of digit ratio.

1.3.2. Associations with testosterone levels

Roney et al. found ambiguous outcomes for sex differences of digit ratios in a captive group of Guinea baboons, but at the same time, they detected lower 2D:4D ratios among males being associated with higher testosterone (2004). In contrast, Lilley et al. found no association between females' 2D:4D and their testosterone or corticosterone levels. Additionally, maternal pre-pregnancy level of testosterone had no influence on offsprings' 2D:4D ratio (2009). Instead, maternal pre-pregnancy corticosterone level was positively correlated with right paws' 2D:4D of progeny.

Cain et al. asserted no association between 2D:4D and testosterone baseline in the dark eyed junco, but found a negative correlation between 2D:4D and elevation of testosterone, in response to a physiological challenge (Cain, Bergeon Burns, & Ketterson, 2012), indicating higher fitness of males with smaller 2D:4D ratios. Once more, this is contradictory to the expectation of birds' patterns of digit ratios.

Burley et al. observed digit ratios in zebra finches to increase simultaneously across egg order with decreasing androgen allocation across the order of laid eggs (2004), but Bodgan did not detect such a relationship (2009).

Hurd et al. investigated intrauterine position effects on digit ratios in male and female mice, hypothesizing that higher testosterone impact of neighboring males would result in smaller digit ratios. Contradictory to the expected outcome, neighboring male fetuses led to increased digit ratios in both sexes (2008). Braña (2008) found that male lizards have longer fourth digits and that during incubation males from "homosex" trios exhibit longer fourth digits than males from "heterosex" trios. Longer fourth digits would result in smaller digit ratios for males and therefore differ from the common patterns of digit ratios in reptiles, being larger for males than females, so Braña.

1.3.3. Association with anogenital distance (AGD)

AGD is often used to sex animals, with males having larger AGDs, and it is known to be influenced by prenatal androgen levels. Hurd et al. (2008) and Manno (2008) found no correlation between AGD and digit ratio in mice, as well as Auger et al. in rats (2013) and Zhao et al. in red squirrels (2014).

1.3.4. Association with fitness

The sexually antagonistic effects of prenatal steroids on general fitness aspects have been addressed by several authors. Body mass as an indicator of fitness was negatively correlated with digit ratio in male barn swallows, whereas it was positively correlated in females (Dreiss et al. 2007). Burley et al. found that females with higher digit ratios (therefore less androgenized) had stronger preferences for an attractive male (2004), but Garamszegi et al. detected no association between digit ratio and actual survival rate of collared flycatchers (Garamszegi, Hegyi, Szöllõsi, Rosivall, Török, Eens, & Møller, 2007).

Navarro et al. predicted sex-specific differences in correlation between immune action and digit ratio and found females with more male-like digit ratios to have weak immune responses (2007). Gooderham and Schulte-Hostedde found digit ratio to be negatively correlated with reproductive output on the one hand, but positively correlated with the amount of parasite load on the other hand (2012).

Tobler et al. detected no association between 3D:4D and endurance of Australian painted dragons, but negative correlations with reaction time (2012). Digit ratio was not correlated with sprint speed or endurance however in the study of Van Damme et al. (2015).

Selective breeding for mice with increased rates of aerobic exercise capacity resulted in increased circulating corticosterone levels and 2D:4D, as consequence of feminization (Yan et al., 2008). In accordance, Talarovicová et al. (2009) described a positive relationship between motor activity and 2D:4D, which was eliminated by that prenatal elevation of testosterone.

1.3.5. Association with secondary sexual character traits

Several authors reported correlations of digit ratio and secondary sexual character traits in birds (Navarro et al. 2007; Dreiss et al. 2007; Garamszegi et al. 2007), which Lombardo et al. (2008) and Ruuskanen et al. (2011) did not. Tobler et al. found an association between digit ratio and a sex-specific morphological trait in the Australian painted dragon (2011).

1.3.6. Association with other morphological traits

A relationship between digit ratio and morphological traits like tail length, badge size, wing length, body size and mass have been discussed by several authors. Some of them reported that

2D:4D is independent of body size (Burley et al. 2004; McIntyre et al. 2006; Chang 2008; Gomes et al. 2011).

Cain et al. on the other hand reasoned that relationships between digit ratio and various measures of body size might be a result of allometry which is the growth trajectory of one part of the body relatively to another (2012); (see also Lombardo et al. 2008; Tobler et al. 2011; Direnzo et al. 2012 and Kaczmarski et al. 2015). Consequently, body size and age might noticeably contribute to the digit ratio trait.

1.3.7. Association with behavioral traits

Different studies examined correlations between digit ratio and behavior. Relationships with fitness and reproductive success are described in *1.3.4. Association with fitness*. Genovart et al. (2008) reported a correlation between digit ratio and monogamy and cooperative breeding in a seabird. Similar results have been reported by Nelson and Shultz: 2D:4D being lower in polygynous species of primates with high intra-sexual competition and being higher in pair-bonded species with low intra-sexual competition (2010). Howlett et al. also found digit ratio in baboons to be negatively correlated with dominance rank and aggression, positively correlated with submission, and not correlated with females' interest in infants or rate of affiliation (2012, 2013). Yan et al. however found no associations with behavioral traits like total daily activity, aggressiveness and anxiety in mice (2009).

1.4. Problem definition

There is large variability across findings about digit ratio research on animal models, since there are differences between and across wider taxonomic groups (as summarized above). Possible influences on outcomes are interspecies differences, measurement methods and certain sample characteristics.

Researchers use diverse measurement approaches: measurements using ruler or calipers as direct methods, digital photographs, scans or X-rays and imprints/stamps or pins as indirect techniques. Several researchers have brought up that there is substantial influence of genetics and heritability on the digit ratio trait. Bailey et al. found no sexual dimorphism, but significant differences between eight inbred strains of mice they used in their study (2004). Further, Forstmeier (2005) found no sex differences in zebra finches, but determined a heritability estimate of 71 to 84% for digit ratio. Nelson and Voracek (2010) found strong familial resemblance in 2D:4D for rhesus macaques as well.

The aim of this review is to determine the amount of sexual dimorphism of all possible combinations of digit ratios for all four limbs by means of meta-analyses. The ambiguous results will be assessed by focusing on interspecies differences and genetic diversity of examined samples as well as on the precision of different measurement approaches.

2. Methods

This review was planned and conducted in accordance with the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analysis (Moher, Liberati, Tetzlaff & Altman, 2009; Liberati et al., 2009).

2.1. Eligibility criteria

Only studies limited to digit ratio research on animals of all taxa reporting sex differences of digit ratios were included into meta-analyses. All types of studies were included except for studies with paleobiological background. No language, geographical or cultural restrictions were applied. Data from experimental approaches could only be included into meta-analyses, if information on male and female control samples was given.

2.2. Search methods

Literature search and collection of data was conducted up to September 2015 by using the electronic databases Web of Science, Biological Sciences, Scopus, GoogleScholar, PsycINFO and the Karlsruhe Virtual Catalog. Search strings were constructed around the terms “digit ratio” and ‘‘animal’’ and adapted for each database as necessary. For example, search strategy was for Biological Sciences: digit ratio AND (animal OR non-human). Additionally, reference lists of identified primary studies or book chapters was searched through manually for further relevant literature.

2.3. Data extractions and management

Data was extracted by using a self-designed data extraction sheet (see *Appendix A*). This data extraction sheet consisted of the following categories: general information like name of author(s), year, status and type of publication, sample information like animal taxa and species, sample size, origin of animals, age, size and weight, information about study design and operational characteristics like type of measurement tools and measurement material (living animal, dead animal, preserved animal or skeleton), as well as information on reliability of measurements (blind to sex and/or body side, measurement technique) and finally the results.

2.4. Data analysis

2.4.1. Assessment of overall effect size

Meta-analyses were conducted separately for all possible combinations of digit ratios including all five digits, using the software Comprehensive Meta-Analysis (CMA) version 3. Standardized mean differences with 95% confidence intervals (*CI*) were computed as the difference in means between groups divided by the pooled standard deviation (*Cohen's d*). Where no standard deviations were given, *Cohen's d* was calculated from standard errors, *t*-values and from *p*-values, where no other information was given.

Data on digit ratios that was averaged for left and right extremities, was included into meta-analyses for both sides each.

2.4.2. Assessment of heterogeneity

To estimate the statistical heterogeneity between studies included into meta-analyses, the *Q*-statistic as well as the I^2-statistic were used. The *Q*-statistic detects the ratio of the observed variation between studies to the within-study error. If the result is significant and the null-hypothesis of a shared common effect size (homogeneity) is rejected, there is heterogeneity between the studies (p. 112, Borenstein, Hedges, Higgins & Rothstein, 2009).

The I^2-statistic is a descriptive statistic of how much variance between studies can be attributed to differences between studies rather than to chance. The magnitude of heterogeneity is categorized as low for *I^2* = 0–24%, moderate for *I^2* = 25–49%, substantial for *I^2* = 50–74% and high for *I^2* = 75–100% (p. 119, Borenstein et al., 2009).

2.4.3. Subgroup and sensitivity analysis

In order to identify influence of possible moderator variables and to explain substantial heterogeneity of effect sizes, subgroup analyses were planned and conducted. Three categorical variables were determined: *animal group* as a higher taxonomic classification of animals (i.e. rodents, primates, reptiles, birds and amphibians), *type of measurement technique* (i.e. using ruler or calipers on living or dead individuals, pins/stamps, osteometric methods, digital photographs or scans and X-rays) and amount of *genetic variance* in the studied sample (i.e. inbred, bred or wild-type).

Further, sensitivity analyses were performed to shed light on the influence of single studies on overall effect size. The effect sizes of studies are combined, while one study is removed in each turn. This allows determining the influence of single studies (p.368, Borenstein et al., 2009). Particular emphasis was laid on study's weight, effect size and on those studies with averaged values for left and right body sides (see *2.4.1. Assessment of overall effect size*).

2.4.4. Risk of bias across studies

A meta-analysis is able to give accurate synthesized information about outcomes of different studies on one research question, but if these studies exhibit biases, the mean effect calculated by meta-analysis will only reflect these biases, too. One such bias is the publication bias, which tells that studies with relatively high effect sizes are more likely to be published than studies with low effect sizes or no effect found (p. 277; Borenstein et al., 2009). Therefore, it is important to deal with biases as systematic errors or deviations from the truth. There are several methods to address publication bias in meta-analysis.

A visual approach is the inspection of the funnel-plot, showing effect size on the X axis and sample size or variance on the Y axis. It reflects the relationship between sample size and effect size. Larger studies are positioned toward the top of the graph and cluster around the mean effect size, as they are considered to be closer to the true effect. Whereas smaller studies appear toward the bottom of the graph because of more sampling error variation of effect sizes. In case of publication bias, the studies, instead of dispersing symmetrically, distribute asymmetrically around the mean effect size (p. 283; Borenstein et al., 2009).

The second possibility to examine the results of meta-analysis, in terms of publication bias, is the Rosenthal's Fail-Safe N. It detects the number of studies with null-results that would be necessary to reach non-significance in the overall effect (p. 284; Borenstein et al., 2009). As a result, it evaluates the robustness of a calculated overall effect size.

Furthermore, the Duval-Tweedie trim-and-fill analysis was conducted, an iterative tool, that removes the most extreme small studies from the positive side of the funnel plot and then computes the effect size once more at each iteration until the funnel plot is symmetric. This is the "new" effect size (p. 286; Borenstein et al., 2009).

3. Results

Meta-analyses were conducted to examine the sexual dimorphism character of digit ratios as a hormonal marker of prenatal androgenization. All possible combinations of digit ratios for all four extremities were calculated, a total of 40 meta-analyses were conducted.

Direction of effect or rather sex difference for calculations was determined as positive, because the occurrence of sexual dimorphism of digit ratio reveals to be discontinuous for sexes. Effect sizes were examined for heterogeneity and were handled consequently under assumption of random-effects model or fixed-effect model for further analyses and interpretations.

In addition, subgroup analyses and sensitivity analyses are focused on 2D:4D digit ratios, but forest and funnel plots for all digit ratios can be found in *Appendices C* and *D*.

3.1. Study selection

Literature search yielded 67 non-duplicate records of which 57 were included into coding procedure. Thirteen studies could not be included into meta-analyses, because of missing data or they did not fit eligibility criteria.

3.2. Study characteristics

A total of 42 primary studies were included into meta-analyses, published between 2002 and 2015. Additionally, two unpublished theses were coded and included into meta-analyses as well. *Figure 1* displays the percentage of investigated animal groups. Seven studies investigated sex dimorphism of digit ratios in primates, fifteen in rodents, eleven in birds, six in reptiles, three in amphibians and one study investigated one species of reptiles and one species of amphibians each. Sixteen studies focused on sex dimorphism of digit ratio alone, but mostly the studies examined associations with hormone levels, behavioral traits, other morphological traits and secondary sexual traits as well. Three studies determined a correlation between digit ratio and anogenital distance (AGD) which is known to be sexually dimorphic. Three studies tried to point out heritability of digit ratio and nine studies used experimental manipulation of prenatal hormonal milieu to investigate postnatal consequences for digit ratio.

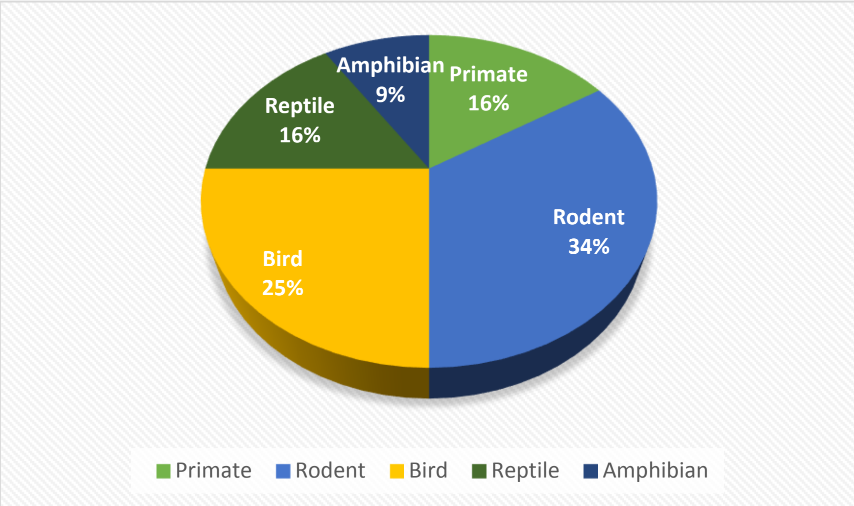

Figure 1: Percentage of animal groups investigated in primary studies

3.3. Excluded studies

Thirteen out of 57 coded studies could not be included into meta-analyses, because of missing data. One study examined digit ratios for fossil hominoids. One study did not report any data to compute effect sizes. The other eleven studies used experimental manipulation and lacked control group data (a detailed list of excluded studies and exclusion criteria can be found in *Appendix B*). One additional study was published after editorial deadline (15.09.2015) and was therefore not included (Olvera-Hernández, S. & Guasti-Fernández, A., 2015).

3.4. *Analyses of overall effects*

A total of 40 meta-analyses were conducted to examine sexual dimorphism for all possible combinations of digit ratios of all four extremities. Table 8 gives an overview of all calculated effect sizes *d*, 95% confidence intervals *CI* and corresponding *p*-values. All funnel plots and forest plots including sensitivity analyses are shown in *Appendices C and D*.

3.5. *Analyses of sex differences for 2D:4D ratios*

3.5.1. *Analysis of heterogeneity for 2D:4D*

Results of analyses of heterogeneity for 2D:4D ratios are listed in Table 1. The *Q*-statistic is not significant for FR 2D:4D (p = .247). This means that there is no heterogeneity between the studies and confirms the assumption of the fixed-effect model. An I^2 of 14.6% indicates low variance of effect sizes. The *Q*-statistic for FL 2D:4D is not significant as well (p = .027), I^2 = 37.4% and indicates moderate inconsistency of effect sizes, therefore the fixed-effect model must be assumed. For HR 2D:4D the test for heterogeneity is highly significant ($p \leq .001$) and there is substantial inconsistency of I^2 = 50.6%, consequently the results must be interpreted under assumption of the random-effects model. This proves a variation among the effect sizes that does not due to random error alone. The *Q*-statistic for HL 2D:4D is not significant (p = .075), there is moderate inconsistency of I^2 = 26.3% and the fixed-effect model can be assumed.

Table 1: Test of Heterogeneity across studies for 2D:4D

	Q	**df (Q)**	**p**	**I²**
FR 2D:4D	45.009	28	.022	37.790
FL 2D:4D	41.532	26	.027	37.397
HR 2D:4D	89.145	44	≤ 0.001*	50.642
HL 2D:4D	48.863	36	.075	26.325

*Weighted sum of squares (Q), degrees of freedom (df), level of significance (p), inconsistencies across study findings (I²); * p ≤ 0.01*

3.5.2. Effect sizes for 2D:4D

Assuming the fixed-effect model analysis of sex differences for 2D:4D ratio of the right front limb (FR 2D:4D) yields a significant effect size of d = 0.239 (95% *CI* [0.178, 0.300]; $p \leq .001$). Thus, it appears that there is a small but significant difference of 2D:4D ratio for the right front limb between the sexes.

For the left front limb (FL 2D:4D) an effect size of d = 0.261 (95% *CI* [0.200, 0.323]; $p \leq .001$) was calculated assuming the fixed-effect model, which resulted likewise in a small but significant difference between the sexes. For the right hind limb (HR 2D:4D) an effect size of d = 0.279 (95% *CI* [0.199, 0.359]; $p \leq .001$) was reached under assumption of the random-effects model, as well a small but significant sex difference in 2D:4D ratio for the right hind limb. In addition a small effect of sexual dimorphism was calculated for the left hind limb (HL 2D:4D) with d = 0.311 (95% *CI* [0.250, 0.373]; $p \leq .001$); (fixed-effect model).

3.5.3. Sensitivity analyses and publication bias for 2D:4D

More detailed analysis of FR 2D:4D indicates a very robust result. The Rosenthal's Fail-Safe-N yields 507 studies showing null-results that would have to be added to effect-size calculation in order to reach non-significance in the overall effect size. Sensitivity analysis indicates no substantial influence on overall effect size of single studies (for forest plots of sensitivity analyses, see *Appendix C*). A visual inspection of the funnel plot for HR 2D:4D indicates asymmetry (Figure 2).

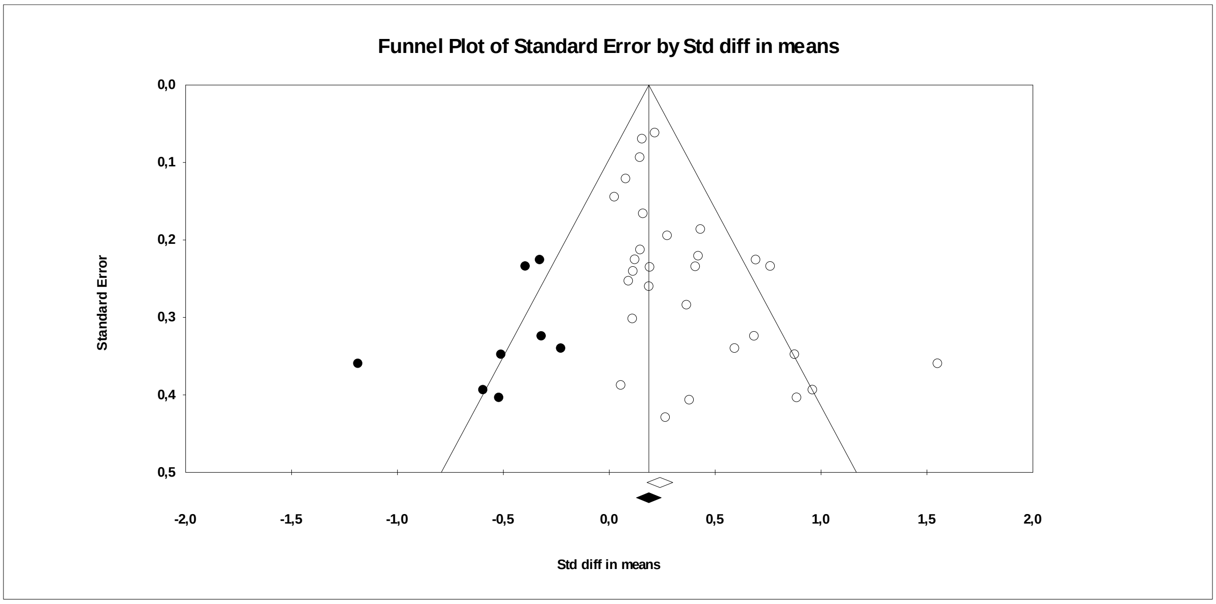

Figure 2: Funnel plot for FR 2D:4D (fixed-effect model)

As can be seen above, there are more studies on the right side of the funnel plot, eight of them very close or beyond the funnel. The trim-and-fill analysis provides information on eight missing studies in overall effect size calculations, requiring an adjustment of the overall effect size to d_{adj} = 0.187 (95% *CI* [0.128, 0.245]).

For FL 2D:4D sensitivity analysis yields no substantial influence of single studies with high or low weight on overall effect size. Rosenthal's Fail-Safe-N calls for 480 further studies showing null-results to reach non-significance in the overall effect size.

The funnel plot shows asymmetry with more studies close or beyond the right side of the funnel (Figure 3). The trim-and-fill analysis demands an adjusted effect size of d_{adj} = 0.205 (95% *CI* [0.147, 0.264]), with seven studies trimmed.

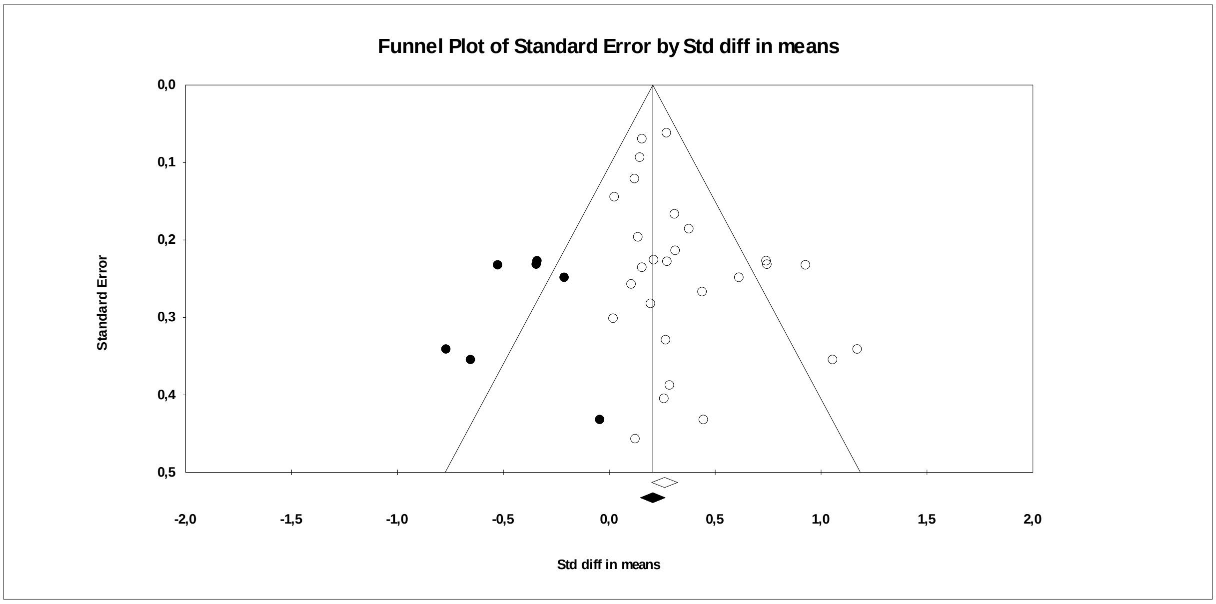

Figure 3: Funnel plot for FL 2D:4D (fixed-effect model)

The overall effect size for HR 2D:4D ratio shows very high robustness with a Rosenthal's Fail-Safe-N of 1050. Additionally, sensitivity analysis disproves substantial influence of single studies on overall effect size. Nevertheless, there is evidence for publication bias, as the inspection of the funnel plot shows (Figure 4). There are more studies on the right side of the funnel and four studies beyond it. Additionally there are two studies beyond the funnel on the left side as well. Consequently an adjusted effect size of d_{adj} = 0.232 (95% *CI* [0.185, 0.279]) was calculated by trim-and-fill-analysis under assumption of the random-effects model.

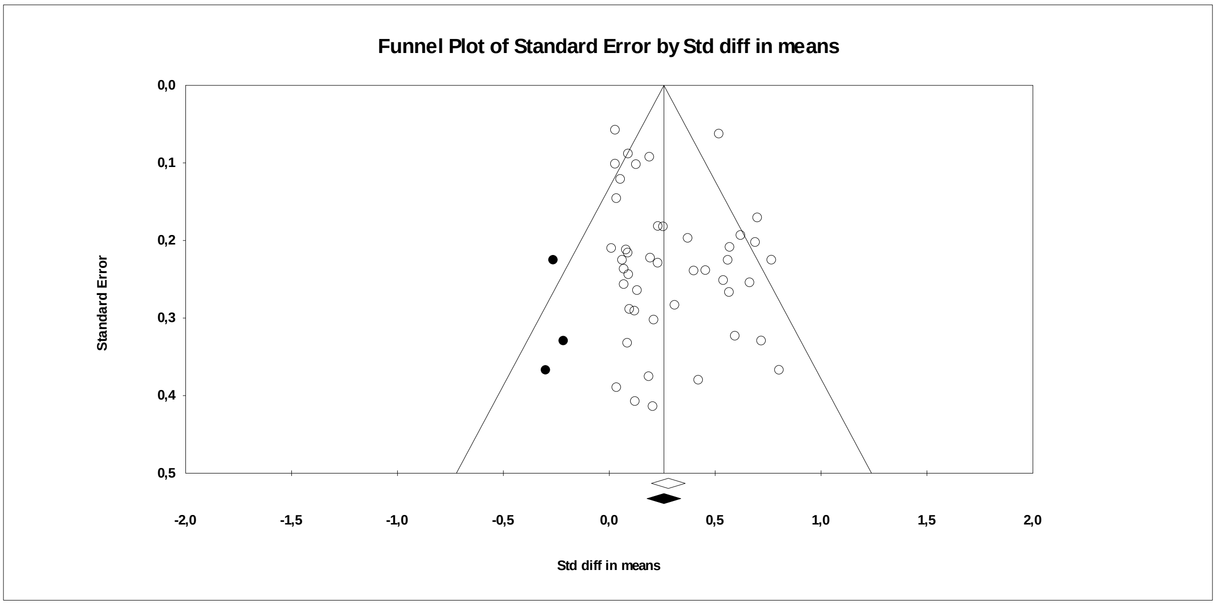

Figure 4: Funnel plot for HR 2D:4D (random-effects model)

Sensitivity analysis for HL 2D:4D provides information that one study with high weight has strong influence on overall effect size. Removing this study with a very large sample size of 1025 individuals by Van Damme, Wijnrocx, Boeye, Huyghe and Van Dongen, (2015), results in an overall effect size of d = 0.260 (95% *CI* [0.189, 0.331]; $p \le .001$). Nevertheless, Rosenthal's Fail-Safe-N of 684 shows a very robust overall effect size. An inspection of the funnel plot displays no major asymmetry (Figure 5). Furthermore, trim-and-fill-analysis requires no adjustment of overall effect size.

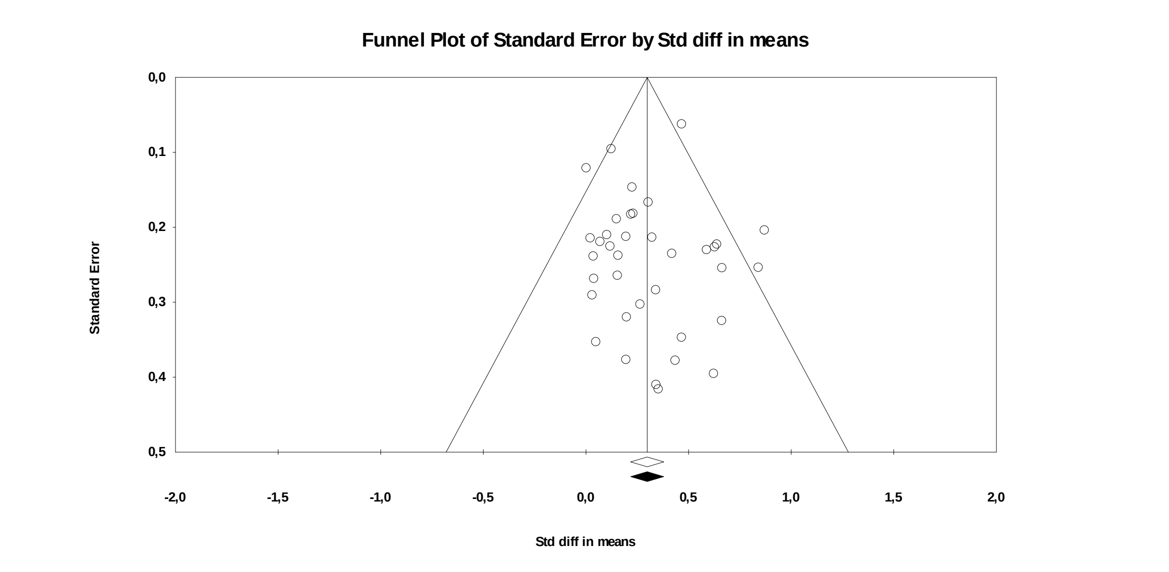

Figure 5: Funnel plot for HL 2D:4D (fixed-effect model)

Since effect sizes for birds are only available for hind limbs, analyses of hind limbs' 2D:4D ratio without effect size data from avian studies, reveal considerable changes in overall effect sizes and publication bias (for forest plots and funnel plots see *Appendices C* and *D*).Overall effect size for HR 2D:4D is then d = 0.316 (95% *CI* [0.254, 0.378], $p \le .001$). *Q*-statistic is not significant and the fixed-effect model can be assumed. Funnel plot is close to symmetry and no adjustments resulting from trim-and-fill-analysis are necessary. For HL 2D:4D an effect size of d = 0.358 (95% *CI* [0.285, 0.430], $p \le .001$) is calculated and approximate symmetry of funnel plot prevails no need for adjustments.

3.5.4. Subgroup Analyses for 2D:4D

Subgroup analyses were conducted to examine the influence of moderator variables and to explain heterogeneity of effect sizes across studies. The *Q*-statistic for HR 2D:4D ratio was highly significant ($p \leq .001$) and exhibited a substantial inconsistency of $I^2 = 50.6\%$. Therefore, analyses of HR 2D:4D were conducted and interpreted assuming the random-effects model. *Q*-statistic was not significant for the other digit ratios though. Subgroup analyses were performed with the moderator variables *animal group* (primate, rodent, bird, reptile, amphibian), *measurement technique* (calipers/ruler, digital, osteometry, stamps/pins/imprints, X-rays) and *level of genetic variance* (inbred strains, breedings, wild type).

Tables 3, 4, 5 and 6 show results of subgroup analyses. There are no significant differences between subgroups of the defined categorical moderators for hind right limb. On the contrary subgroups of *animal group* ($Q = 13.785$, $p = .008$) and *genetic variance* ($Q = 8.365$, $p = .015$) are significantly different for HL 2D:4D. For FR 2D:4D subgroups of *genetic variance* ($Q = 13.891$, $p = .001$) and for FL 2D:4D subgroups of *measurement techniques* ($Q = 13.909$, $p = .003$) differ significantly.

Reptiles and amphibians show the largest effect sizes, whereas primates show the smallest. It is apparent from the tables that primates exhibit the smallest and non-significant sex differences in the feet (right: $d = 0.064$, $p = .760$; left: $d = 0.186$, $p = .314$) and small but significant differences in the hands (right: $d = 0.187$, $p = .001$; left: $d = 0.179$, $p = .002$). Effects sizes for rodents do not differ much between hind (right: $d = 0.231$, left: $d = 0.195$) and front limbs (right: $d = 0.240$, left: $d = 0.199$), but are larger for right limbs. Further, the feet of birds exhibit small significant effect sizes (for right: $d = 0.214$, $p = .000$; for left: $d = 0.225$, $p = .004$) that do not show considerable asymmetry. Reptiles show larger significant effect sizes for hind limbs (right: $d = 0.410$, left: $d = 0.442$) than for front limbs (right: $d = 0.240$, left: $d = 0.279$) and larger effects for left than for right limbs. Effect sizes for amphibians on the contrary, are slightly larger for front limbs (right: $d = 0.380$, left: $d = 0.496$) than for rear limbs (right: $d = 0.325$, left: $d = 0.423$), but also larger for left than for right. An overview of effect sizes for 2D:4D ratios for animal groups is given in the following table.

Table 2: Effect sizes *d* and *p*-values for sex differences of animal groups

	HR 2D:4D	HL 2D:4D	FR 2D:4D	FL 2D:4D
Primates	0.065 (.760)	0.186 (.314)	0.187 (.001)	0.179 (.002)
Rodents	0.250 (≤ .001)	0.195 (≤ .001)	0.240 (.004)	0.199 (.021)
Birds	0.214 (≤ .001)	0.225 (.004)	-	-
Reptiles	0.410 (≤ .001)	0.442 (≤ .001)	0.240 (≤ .001)	0.279 (≤ .001)
Amphibians	0.320 (≤ .001)	0.423 (≤ .001)	0.380 (≤ .001)	0.496 (≤ .001)

Subgroups of *measurement techniques* only show heterogeneity for FL 2D:4D. Wide confidence intervals and high variance for osteometry, pins/stamps/imprints and X-rays and narrow confidence intervals and small variance for calipers/ruler and digital photographs/scans indicate more accuracy for measurements with the last two mentioned.

Sexual dimorphism seems more pronounced in wild type animals and breedings than in inbred animals. Inbred animals show very small and non-significant effect sizes, whereas wild type animals show larger significant effect sizes for hind limbs (right: d = 0.302, left: d = 0.369) and breedings show larger significant effect sizes for front limbs (right: d = 1.078, left: d = 0.366).

Table 3: Subgroup analyses for 2D:4D of hind right limbs

	Random-effects model			Fixed-effect model			Total between
Subgroups	N	d (p)	95% CI	d (p)	95% CI	I²	Q (p)
Animal group							4.976 (.290)
Primate	2	0.065 (.760)	[-0.351, 0.480]	0.057 (.756)	[-0.304, 0.418]	0.000	
Rodent	15	0.250 (≤ .001)	[0.177, 0.382]	0.209 (≤ .001)	[0.108, 0.311]	15.862	
Bird	15	0.214 (≤ .001)	[0.094, 0.334]	0.134 (≤ .001)	[0.061, 0.208]	47.137	
Reptile	6	0.410 (≤ .001)	[0.246, 0.575]	0.430 (≤ .001)	[0.337, 0.524]	63.545	
Amphibian	8	0.325 (.001)	[0.130, 0.520]	0.329 (≤ .001)	[0.158, 0.500]	9.427	
Measurement							5.180 (.269)
Calipers	17	0.384 (≤ .001)	[0.259, 0.508]	0.290 (≤ .001)	[0.228, 0.325]	74.919	
Digital	21	0.216 (≤ .001)	[0.097, 0.335]	0.178 (≤ .001)	[0.097, 0.259]	0.000	
Osteometry	1	0.015 (.956)	[-0.523, 0.553]	0.015 (.943)	[-0.399, 0.429]	0.000	
Pins	1	0.137 (.667)	[-0.486, 0.760]	0.137 (.606)	[-0.384, 0.658]	0.000	
X-rays	5	0.204 (.163)	[-0.082, 0.491]	0.198 (.101)	[-0.038, 0.435]	0.000	
Genetics							3.375 (.185)
Breeding	15	0.294 (≤ .001)	[0.164, 0.424]	0.173 (≤ .001)	[0.098, 0.247]	55.576	
Inbred	3	0.053 (.681)	[-0.198, 0.303]	0.052 (.548)	[-0.118, 0.222]	0.000	
Wild Type	27	0.302 (≤ .001)	[0.201, 0.403]	0.329 (≤ .001)	[0.262, 0.396]	39.576	

Number of included studies (N), Effect size (d), 95%-Confidence intervals for Cohen's d (CI), Weighted sum of squares (Q), level of significance (p), inconsistencies across study findings (I²)

Table 4: Subgroup analyses for 2D:4D of hind left limb

	Fixed-effects model			Heterogeneity			Total between
Subgroups	N	d (p)	95% CI	Q	p	I^2	Q (p)
Animal group							13.785 (.008)
Primate	2	0.186 (.314)	[-0.176, 0.548]	0.588	.443	0.000	
Rodent	13	0.195 (≤ .001)	[0.090, 0.300]	16.751	.159	28.363	
Bird	9	0.225 (.004)	[0.073, 0.376]	5.762	.674	0.000	
Reptile	5	0.442 (≤ .001)	[0.335, 0.550]	3.029	.553	0.000	
Amphibian	8	0.423 (.001)	[0.255, 0.591]	8.947	.256	21.765	
Measurement							8.755 (.119)
Calipers	10	0.278 (≤ .001)	[0.125, 0.432]	6.736	.665	0.000	
Digital	20	0.308 (≤ .001)	[0.236, 0.380]	30.248	.049	37.187	
Osteometry	1	0.107 (.613)	[-0.307, 0.521]	0.000	1.000	0.000	
Pins	1	0.200 (.597)	[-0.541, 0.941]	0.000	1.000	0.000	
X-rays	4	0.312 (.021)	[0.047, 0.577]	3.124	.373	3.955	
Genetics							8.365 (.015)
Breeding	10	0.271 (≤ .001)	[0.143, 0.399]	19.194	.166	36.592	
Inbred	3	0.101 (.245)	[-0.069, 0.272]	1.363	.506	0.000	
Wild Type	24	0.369 (≤ .001)	[0.292, 0.446]	24.942	.535	7.784	

Number of included studies (N), Effect size (d), 95%-Confidence intervals for Cohen's d (CI),Weighted sum of squares (Q), level of significance (p), inconsistencies across study findings (I^2)

Table 5: Subgroup analyses for 2D:4D of front right limb

	Fixed-effect model			Heterogeneity			Total between
Subgroups	N	d (p)	95% CI	Q	p	I²	Q (p)
Animal group							3.068 (.381)
Primate	7	0.187 (.001)	[0.077, 0.298]	7.251	.298	17.248	
Rodent	7	0.240 (.004)	[0.079, 0.402]	17.514	.008	65.741	
Reptile	8	0.240 (≤ .001)	[0.149, 0.331]	8.587	.284	18.485	
Amphibian	7	0.380 (≤ .001)	[0.195, 0.566]	8.589	.198	30.146	
Measurement							6.581 (.087)
Calipers	8	0.159 (.001)	[0.063, 0.254]	5.358	.616	0.000	
Digital	17	0.286 (≤ .001)	[0.203, 0.370]	21.973	.144	27.185	
Osteometry	1	0.151 (.480)	[-0.268, 0.570]	0.000	1.000	0.000	
X-rays	3	0.486 (.002)	[0.177, 0.794]	11.097	.004	81.977	
Genetics							13.891 (.001)
Breeding	2	1.078 (≤ .001)	[0.604, 1.551]	3.175	.075	68.501	
Inbred	2	0.093 (.390)	[-0.118, 0.304]	0.028	.868	0.000	
Wild Type	25	0.237 (≤ .001)	[0.173, 0.301]	27.915	.264	14.025	

Number of included studies (N), Effect size (d), 95%-Confidence intervals for Cohen's d (CI),Weighted sum of squares (Q), level of significance (p), inconsistencies across study findings (I²)

Table 6: Subgroup analyses for 2D:4D of front left limb

	Fixed-effect model			Heterogeneity			Total between
Subgroups	N	d (p)	95% CI	Q	p	I^2	Q (p)
Animal group							8.778 (.032)
Primate	6	0.179 (.002)	[0.067, 0.291]	3.142	.678	0.000	
Rodent	6	0.199 (.021)	[0.030, 0.367]	8.962	.111	44.211	
Reptile	8	0.279 (≤ .001)	[0.188, 0.370]	10.987	.139	36.289	
Amphibian	7	0.496 (≤ .001)	[0.308, 0.685]	9.662	.140	37.904	
Measurement							13.909 (.003)
Calipers	8	0.158 (.001)	[0.064, 0.253]	2.384	.936	0.000	
Digital	17	0.324 (≤ .001)	[0.241, 0.407]	25.238	.066	36.604	
Osteometry	1	0.317 (.140)	[-0.104, 0.738]	0.000	1.000	0.000	
X-rays	1	1.176 (.001)	[0.505, 1.847]	0.000	1.000	0.000	
Genetics							1.633 (.442)
Breeding	3	0.366 (.022)	[0.052, 0.681]	7.165	.028	72.087	
Inbred	2	0.145 (.178)	[-0.066, 0.356]	0.123	.726	0.000	
Wild Type	22	0.268 (≤ .001)	[0.202, 0.334]	32.611	.051	35.605	

Number of included studies (N), Effect size (d), 95%-Confidence intervals for Cohen's d (CI),Weighted sum of squares (Q), level of significance (p), inconsistencies across study findings (I^2)

3.6. Analyses of sex differences for 2D:3D

3.5.1. Analysis of heterogeneity for 2D:3D

Table 7 shows the results of tests for heterogeneity for 2D:3D ratios. There is no significant *Q*-statistic for any digit ratio, therefore the Fixed-Effect-Model is assumed for all meta-analyses.

Table 7: Test of Heterogeneity across studies for 2D:3D

	Q	df (Q)	p	I²
FR 2D:3D	11.599	9	.237	22.408
FL 2D:3D	13.109	8	.108	38.971
HR 2D:3D	6.820	10	.742	0.000
HL 2D:3D	6.932	8	.544	0.000

Weighted sum of squares (Q), degrees of freedom (df), level of significance (p), inconsistencies across study findings (I^2)

For FR 2D:3D ratio a small but significant effect size of *d* = 0.279 (95 % *CI* [0.176, 0.382]; *p* ≤ .001) was calculated. The analysis of FL 2D:3D with *d* = 0.303 (95 % *CI* [0.199, 0.408]; *p* ≤ .001) shows a small significant result as well.

Effect sizes for hind limbs' 2D:3D indicate small but significant sexual dimorphism for the right side: *d* = 0.269 (95 % *CI* [0.181, 0.356]; *p* ≤ .001) and for the left side: *d* = 0.266 (95 % *CI* [0.166, 0.367]; *p* ≤ .001). Sensitivity analyses for all 2D:3D ratios yield a high influence on overall effect size of one study by Van Damme et al. (2015). All forest and funnel plots as well as forest plots for sensitivity analyses are given in *Appendices C* and *D*.

Table 8: Effect sizes *d* for all combinations of digit ratios for all extremities, 95 % Confidence Intervals *CI*, *p*-values for overall effects

		2D	3D	4D	5D
Hind right limb	1D	0.211 (-0.060, 0.483), *p* = .127	0.098 (-0.095, 0.292), *p* = .319	0.102 (-0.170, 0.374), *p* = .461	0.231 (-0.042, 0.503), *p* = .012
	2D		0.269 (0.181, 0.356); *p* ≤ .001	0.279 (0.199, 0.359), *p* ≤ .001 *	0.328 (0.119, 0.537), *p* = .002
	3D			0.224 (0.140, 0.309), *p* ≤ .001	0.234 (0.026, 0.443), *p* = .028
	4D				0.370 (0.161, 0.579), *p* = .001
Hind left limb	1D	0.208 (-0.064, 0.480), *p* = .135	0.112 (-0.081, 0.306), *p* = .225	0.156 (-0.116, 0.428), *p* = .262	0.349 (0.077, 0.626), *p* = .097
	2D		0.266 (0.166, 0.367), *p* ≤ .001	0.311 (0.250, 0.373), *p* ≤ .001	0.332 (0.124, 0.541), *p* = .002
	3D			0.315 (0.218, 0.411), *p* ≤ .001	0.221 (0.012, 0.429), *p* = .038
	4D				0.345 (0.135, 0.554), *p* = .001
Front right limb	1D	0.368 (0.095, 0.640), *p* = .008	0.459 (0.186, 0.731), *p* = .001	0.360 (0.080, 0.632), *p* ≤ .001	0.288 (0.015, 0.560), *p* = .038
	2D		0.279 (0.176, 0.382), *p* ≤ .001	0.239 (0.178, 0.300), *p* ≤ .001	0.341 (0.120, 0.561), *p* = .002
	3D			0.367 (0.131, 0.602), *p* = .002	0.462 (0.240, 0.684), *p* ≤ .001
	4D				0.690 (0.464, 0.916), *p* ≤ .001
Front left limb	1D	0.373 (0.101, 0.646), *p* = .007	0.309 (0.038, 0.580), *p* = .026	0.201 (-0.070, 0.471), *p* = .147	0.231 (-0.041, 0.503), *p* = .096
	2D		0.303 (0.199, 0.408), *p* ≤ .001	0.261 (0.200, 0.323), *p* ≤ .001	0.355 (0.125, 0.586), *p* = .003
	3D			0.112 (0.008, 0.216), *p* = .035	0.419 (0.187, 0.651), *p* ≤ .001
	4D				0.360 (0.129, 0.591), *p* = .002

* analysis assuming random-effects model

3.6. Analysis of sex differences for 2D:5D

3.6.1. Analysis of heterogeneity for 2D:5D

Table 9 shows the results of tests for heterogeneity for 2D:5D ratios. *Q*-statistic is not significant for any ratio and there is no or moderate inconsistency. The fixed-effect model is assumed for all ratios.

Table 9: Test of Heterogeneity across studies for 2D:5D

	Q	df (Q)	p	I^2
FR 2D:5D	4.906	5	.427	0.000
FL 2D:5D	2.532	4	.639	0.000
HR 2D:5D	9.379	4	.052	57.353
HL 2D:5D	7.874	4	.096	49.200

Weighted sum of squares (Q), degrees of freedom (df), level of significance (p), inconsistencies across study findings (I^2)

There are small sex differences in 2D:5D for all four limbs. The front right limb shows an effect size of d = 0.341 (95% *CI* [0.120, 0.561]; p = .002). For the front left limb an effect size of d = 0.355 (95% *CI* [0.125, 0.586]; p = .003) is calculated. The right hind limb reaches an effect size of d = 0.328 (95% *CI* [0.119, 0.537]; p = .002) and the left hind limb an effect size of d = 0.332 (95% *CI* [0.124, 0.541]; p = .002).

3.7. Analysis of sex differences for 3D:4D

3.7.1. Analysis of heterogeneity for 3D:4D

There is no heterogeneity for 3D:4D ratios, therefore, results can be interpreted under assumption of the fixed-effect model. I^2-statistic indicates low or moderate inconsistencies (Table 10).

Table 10: Test of Heterogeneity across studies for 3D:4D

	Q	df (Q)	p	I²
FR 3D:4D	19.420	9	.022	53.655
FL 3D:4D	15.767	8	.046	49.262
HR 3D:4D	13.337	11	.272	17.525
HL 3D:4D	4.688	9	.861	0.000

Weighted sum of squares (Q), degrees of freedom (df), level of significance (p), inconsistencies across study findings (I^2)

There are small and significant sex differences for 3D:4D for all four extremities. For front right limb an effect size of *d* = 0.367 (95% *CI* [0.131, 0.602]; *p* = .002) and for front left limb an effect size of *d* = 0.287 (95% *CI* [0.071, 0.503]; *p* = .009) are determined.

For hind right limb an effect size of *d* = 0.224 (95% *CI* [0.116, 0.332], *p* ≤ .001) and for hind left limb an effect size of *d* = 0.315 (95% *CI* [0.218, 0.411]; *p* ≤ .001) are calculated.

3.8. Analysis of sex differences for 3D:5D

3.8.1. Analysis of heterogeneity for 3D:5D

Q-statistic and I^2-statistic are shown in Table 11. No heterogeneity for 3D:5D digit ratios is detected.

Table 11: Test of Heterogeneity across studies for 3D:5D

	Q	df (Q)	p	I²
FR 3D:5D	4.906	5	.427	0.000
FL 3D:5D	2.532	4	.639	0.000
HR 3D:5D	9.379	4	.052	57.353
HL 3D:5D	7.874	4	.096	49.200

Weighted sum of squares (Q), degrees of freedom (df), level of significance (p), inconsistencies across study findings (I^2)

Front limbs show a tendency to medium significant effect sizes, for front right $d = 0.462$ (95% *CI* [0.240, 0.684]; $p \leq .001$) and for front left $d = 0.419$ (95% *CI* [0.187, 0.651]; $p = .004$). There are small but still significant effect sizes for hind limbs as well. For hind right limb $d = 0.234$ (95% *CI* [0.026, 0.443]; $p = .028$) and for left hind limb $d = 0.221$ (95% *CI* [0.012, 0.429]; $p = .038$).

3.9. Analysis of sex differences for 4D:5D

3.9.1. Analysis of heterogeneity for 4D:5D

Results of tests for heterogeneity are shown in Table 12. *Q*-statistic is not significant for any ratio and there is no till medium inconsistency across effect sizes.

Table 12: Test of Heterogeneity across studies for 4D:5D

	Q	df (Q)	p	I²
FR 4D:5D	8.533	5	.129	41.406
FL 4D:5D	3.211	4	.523	0.000
HR 4D:5D	6.845	4	.144	41.563
HL 4D:5D	8.983	4	.062	55.472

Weighted sum of squares (Q), degrees of freedom (df), level of significance (p), inconsistencies across study findings (I^2)

The front right limb shows a medium to high effect size of $d = 0.690$ (95% *CI* [0.464, 0.916]; $p \leq .001$). The front left limb shows a small effect size of $d = 0.360$ (95% *CI* [0.129, 0.591]; $p = .002$). Small effect sizes are determined for hind limbs as well: for HR 4D:5D $d = 0.370$ (95% *CI* [0.161, 0.579]; $p = .001$) and for HL 4D:5D $d = 0.345$ (95% *CI* [0.135, 0.554]; $p = .001$).

3.10. Analyses of sex differences for digit ratios including the first digit

3.10.1. Analyses of sex differences for digit ratios combining the first digit

No heterogeneity was detected for any digit ratio including the first digit. Therefore, the fixed-effect model is chosen for meta-analyses. All results are shown in Table 13.

Table 13: Test of Heterogeneity across studies for digit ratios 1D-5D

	Q	df (Q)	p	I^2
FR 1D:2D	0.897	2	.639	0.000
FL 1D:2D	0.831	2	.660	0.000
HR 1D:2D	0.392	2	.822	0.000
HL 1D:2D	0.843	2	.656	0.000
FR 1D:3D	0.573	2	.751	0.000
FL 1D:3D	0.673	2	.714	0.000
HR 1D:3D	0.666	3	.881	0.000
HL 1D:3D	1.116	3	.773	0.000
FR 1D:4D	1.420	2	.492	0.000
FL 1D:4D	1.237	2	.539	0.000
HR 1D:4D	0.060	2	.970	0.000
HL 1D:4D	0.645	2	.724	0.000
FR 1D:5D	0.077	2	.962	0.000
FL 1D:5D	1.876	2	.390	0.000
HR 1D:5D	0.285	2	.867	0.000
HL 1D:5D	2.237	2	.327	10.602

Weighted sum of squares (Q), degrees of freedom (df), level of significance (p), inconsistencies across study findings (I^2)

4. Discussion

4.1. Effect sizes for sexual dimorphism of digit ratios

The first question in this review aims to determine sex differences for all digit ratio combinations. Overall effect sizes are small in general, except for FR 1D:3D (d = 0.459, p = .001) and FR 4D:5D (d = 0.690, $p \leq .001$). They range from d = 0.098 (p = .319) for HR 1D:3D to d = 0.690 ($p \leq .001$) for FR 4D:5D. Digit ratios including the fifth digit exhibit the highest effect sizes. Conflicting previous literature, the results provide no information on patterns of laterality. However, data indicates differences along the antero-posterior axis, effect sizes tending to be larger for front limbs. Admittedly, this pattern inverts (at least for 2D:4D ratios) when not taking into account birds' data, indicating that birds show less sex dimorphism in digit ratios and contribute substantially to overall effect sizes.

4.2. Interspecies differences of digit ratios

Results of subgroup analyses suggest differences between animals of wider taxonomic groups, although evidence for heterogeneity was found only for HR 2D:4D.

For all 2D:4D ratios primates show the smallest sex differences, which are not significant for feet. Likewise, McFadden and Shubel (2002) found generally smaller sex differences in human toes (cited by Voracek, 2006). Inconsistencies of effect sizes are smallest for primates in comparison to other animal groups though, suggesting less variability in digits' characteristics for this group. Rodents seem to express similar sex differences in digit ratios for all four limbs, being larger for right limbs (supporting the observation that digit ratios are pronounced stronger on the right side) and only slightly larger for front limbs.

Birds exhibit small sex differences as well, being slightly larger for left feet. Chang (2006) pointed out that avian species share a common ancestor with reptiles; and following evolutionary relatedness, both exhibit similar patterns of digit ratio, being larger in males than in females. The amount of sexual dimorphism in this trait however is dissimilar for the two groups, being much larger for reptiles than birds. Burley and Foster (2004) were the first reporting avian digit ratios. Since then results on birds' digit ratios are inconsistent as summarized in *1.3. Current state of research*, but when sexual dimorphism is reported, it is smaller for females than for males. In birds, females are the heterogametic sex (ZW), whereas in mammals it is the male (XY). It seems likely to explain these opposite patterns between mammals and birds. Lombardo et al. (2008) investigated digit ratios in four species of birds from three taxonomic orders (Passeriformes, Pscittaciformes and Galliformes). When analyzed separately, they did not detect sex differences in 2D:4D, but pooling data from all four species resulted in larger 2D:4D and 2D:3D for males, although effect sizes were small. The authors suggested to consider certain difficulties in examining digit ratios in birds, such as: complexities in hormonal exposure from embryonic and maternal origin, sex determination by heterogametic females rather than males in mammals, generally smaller digit ratios for toes than for fingers and strong natural selection for certain shapes of feet that may counteract the effects of hormones on digit ratio development. Inconsistencies of effect sizes for birds' 2D:4D ratios are moderate for right feet and null for left feet however, indicating homogeneity of sexual dimorphism in this group.

Reptiles and amphibians exhibit larger significant small to medium effect sizes or rather sex dimorphism of digit ratios. This result is in accordance with considerations about the phylogenetic constraint of this trait, reptiles and amphibians being the elder phylogenetic taxa.

Patterns of digit ratios in reptiles vary among species (see Rubolini et al. 2006; Direnzo and Stynosky 2012, Lombardo et al. 2008; Gomes and Kohlsdorf 2011; Van Damme et al. 2015), and different populations of the same species (Chang et al. 2006; Lombardo et al. 2008). Lombardo et al. (2008), Gomes and Kohlsdorf (2011), as well as Van Damme et al. (2015) emphasize possible interacting effects of selection for adapted digits to different environments and functions: habitat use and locomotor behavior may override developmental patterns of digit ratio. In addition, Direnzo et al. (2012) point out to consider chromosomal sex determination systems in reptiles that differ among these taxa. Nevertheless, inconsistencies of effect sizes for 2D:4D are small to medium, indicating no greater heterogeneity in this group.

Amphibians were investigated firstly by Chang et al. (2008), detecting a significantly higher 2D:4D ratio in the hind limbs of male strawberry poison dart frogs. Direnzo and Stynoski (2012) found higher 2D:4D ratios in the front limbs of the strawberry dart frog and a higher 2D:4D ratio in the left forelimb of male Bransford's robber frog.

Chang et al. (2008) suggested that amphibians expressing a pattern in which 2D:4D is larger in males than in females, would show that this pattern as seen in studies of diapsid birds and reptiles would be the ancestral state of the digit ratio trait. Kaczmarski et al. recently found a mammalian-like 2D:4D ratio in newts (2015). A lower 2D:4D ratio for males was identified in three species of newts (for all four limbs of Alpine newts - *Ichtyosaura alpestris*, for rear limbs of Carpathian newts – *Lissotriton* *montandoni* and for rear limbs of smooth newts – *Lissotriton vulgaris*). No sexual dimorphism of 2D:4D ratio was found for northern crested newts – *Triturus cristatus*.

Balogová et al. analyzed digit ratios in the fire salamander, a common amphibian in Central and Southern Europe (2015) and found a nonsignificant trend towards males having a lower 2D:3D ratio than females. No sex differences in other ratios have been detected (Balogová, Nelson, Uhrin, Figurová, Ledecký & Zyśk, 2015).

Information on small variances and inconsistencies of effect sizes for amphibians and reptiles are surprisingly tough. Smaller animals with smaller extremities are anticipated to show larger measurement errors. Nevertheless, most studies, examining reptiles and amphibians, use digital photographs or scans for measurements (thirteen out of nineteen samples were measured with digital approaches) which tend to be more accurate and precise than others (Voracek et al., 2007).

4.3. Genetic variances of samples

Examined samples of animals vary in their extend of genetic diversity. Some studies use laboratory animals like mice, rats or rhesus macaques, which are either bred or inbred. Other authors use captured wild type animals. Subgroup analyses indicate differences of effect sizes between animals of these three groups. The most obvious finding to emerge from the analyses is that inbred animals show the smallest and not significant effect sizes for all 2D:4D ratios with generally no inconsistency. This finding is in accordance with Bailey et al. who found no sexual dimorphism of the digit ratio trait but differences between the eight inbred mouse strains (2004) and supposed the assumption of substantial heritability of the digit ratio trait.

For hind limbs sex dimorphism of 2D:4D ratio is more pronounced in wild type animals than in bred animals, whereas for front limbs it is more pronounced in breedings than in wild type animals. Additionally, there is more heterogeneity and inconsistency of effect sizes for breedings than for captured wild animals. The results are contrary to expectations of more genetic diversity and therefore more heterogeneity of effect sizes expressed in wild animals. For effect sizes of front limbs however the number of samples of bred animals is very small (two and three samples for breedings versus twenty-five and twenty-two for wild type animals). Besides information on origin and extent of genetic diversity of breedings is very little so that no homogeneity of genetic variance can be assumed for this group.

4.4. Evaluation of measurement methods

Focusing details of subgroup analyses lead to conclusions that measurements with digital approaches and measurements with calipers generate less variance and inconsistency across effect sizes, while measurements with osteometric methods, X-rays and indirect approaches, such as measurements of imprints and pins result in large variances, inconsistencies and confidence intervals and therefore are less precise and not recommended for digit measurements. X-ray approaches imply complexities regarding the decision of measuring whole rays versus summing the length of single phalanges of rays, neglecting impact of either soft tissue or both, soft tissue and interphalangeal joint space. This might lead to the high variability of effect sizes for measurements with X-rays in the data.

The fact that measurements with calipers seem as reliable as digital techniques might be surprising, but most studies using calipers measured digits of either anesthetized or dead animals, therefore measurement error due to agility of animals might be small.

4.5. Limitations and implications for further research

There are several limitations regarding this review, notably the substantial heterogeneity of study results. As described in *1.3. Current state of research*, findings about sexual dimorphism of the digit ratio trait are very ambiguous, not only between different taxa but also across taxa.

Certain aspects of animal samples could explain the amount of heterogeneity: interspecies differences have been assessed in this review, but could not contribute to fully elucidate the heterogeneity of effect sizes. Difficulties result from interspecies' differences in patterns and timings of early testosterone production and patterns and timings of digit development, from natural selection of specialized extremities as well as variability of sex determination systems across amphibians and reptiles.

The impact of genetic diversity of samples could not be determined sufficiently, because information on amount of genetic variability of samples was rare, especially for bred animals. The three broad categories of *inbred*, *bred* and *wild animals* were built disregarding further information on origin of population and genetic background or breeding history of animals. Therefore, findings about the influence of genetics on digit ratio implicate certain differences between the groups, but could not clear out heterogeneity of effect sizes. In addition the numbers of studies for inbred and bred animals are very small in relation to the number of wild animals. This leads to further limitations for interpretation.

Literature indicates substantial influence of sex dimorphism of body size on digit ratio. Unfortunately, only few studies took this into account, while most studies did not report any information on body size for their samples. Hence, this aspect was not assessed in this review, but comprises implications for future concerns about digit ratio research.

The details of molecular mechanisms of digit development are not fully resolved and therefore it is important for research into animal models to consider continuance of measurement material. Heterogeneity of outcomes could be based on differences between measurements of skeletons, preserved animals or living animals.

Besides, there are differences between precision and reliability of measurement approaches. Measurements of fixed extremities are more reliable than measurements on agile animals or indirect measurement approaches like imprints or pins (used in several bird studies). In their report on repeatability and interobserver error of digit ratio measurements Voracek et al. pointed out that even experts in the digit ratio research are susceptible to mistakes in measurement procedures. They gave some practical recommendations: data should base on averages from two or three measurements; and absolute-agreement intraclass correlation (ICC) instead of Pearson correlation or Cronbach's alpha coefficient should be used for repeatability assessment (2007).

4.6. Conclusions

This review was conducted to determine the amount of sex differences for digit ratios from animal studies and to discover underlying parameters that have either influence on development of the trait or interfere with precise detection of the trait.

Sex differences for digit ratios in animals are small and vary between and across taxa. Research findings and interspecies comparisons are confound by differences in patterns and timings of phylogeny and ontogeny of species. Evidence from experimentation on the effects of prenatal androgens in animals presents an important source of elucidation about the effects in humans. Nevertheless, the usability of animal models for studying patterns and mechanisms of prenatal androgen affection on behavioral sex differences remains limited, because of the mentioned noticeable developmental differences between species.

Further studies on animal models should therefore focus on determining factors of the digit ratio trait, which are ontogenetic characteristics like sex determination systems, adaptations of extremities to environmental conditions and sex dimorphism of size. In addition, sample characteristics must be considered with regard to genetic variability. Besides more attention to measurement approaches and recommendations on reliability is necessary.

5. Summary

Since the ratio of the second-to-fourth finger length is known and proposed as a marker for prenatal sex hormones, this phenomenon is intensely studied. Especially the individual differences research as well as medicine are interested to resolve the influence of the prenatal hormonal milieu on cognitive and behavioral traits. There is a growing body of literature studying digit ratio in animals since 2002.

The aim of this review was to summarize findings about animal studies on digit ratio and to determine the amount of sex dimorphism of this trait for all extremities and all combinations of digit ratios by means of meta-analyses.

A number of 56 primary studies for qualitative and a number of 44 studies for quantitative synthesis was identified. Research findings are very ambiguous and therefore several confounding factors have been examined: taxonomic group, genetic diversity of animal sample as well as measurement approaches.

Overall sex differences are small, except for 4D:5D of the front right limb and several digit ratios tend to be of medium size. In general, sex differences for front limbs and digit ratios including the fifth finger tend to be larger.

Animal groups (primates, rodents, birds, reptiles and amphibians) differ in their amount of sex dimorphism of digit ratios, although they are not significantly different. Reptiles and amphibians show larger sex differences, whereas primates show smallest sex differences.

Furthermore, there is evidence for substantial influence of genetic variability across animal samples on digit ratio and for heritability of the digit ratio trait.

Moreover, strong impact comes from measurement approaches: measurements with digital techniques and calipers/ruler – at least for animals that do not move - are more reliable than osteometry or measurements of X-rays and indirect methods like imprints/stamps or pins.

Since the examined species differ in phylogenetic and ontogenetic characteristics, a generalization of the findings from animal studies on human population is restricted. The pattern and timing of differentiation of fingers, the amount and timing of hormonal impact and responsiveness of tissues differ noticeably between species.

Zusammenfassung

Seit der Entdeckung von Geschlechtsunterschieden im Fingerlängenverhältnis zwischen Zeige- und Ringfinger, sowie der Vermutung, dass dieser Geschlechtsunterschied auf den Einfluss pränataler Geschlechtshormone zurückzuführen ist, wird dieses Phänomen intensiv erforscht. Das Ausmaß interindividueller Unterschiede infolge pränataler Hormoneinflüsse ist für psychologische sowie medizinische Forschungsfelder von Interesse. Um detailliertere Kenntnisse über die Entstehungsbedingungen des Fingerlängenverhältnisses zu gewinnen, sind seit 2002 viele Tierstudien durchgeführt worden.

Ziel dieser Arbeit war es die Forschungsergebnisse der Tierstudien zu 2D:4D und anderen Fingerlängenverhältnissen zusammenzutragen und die Größe der Geschlechtsunterschiede aller möglichen Kombinationen von Fingerlängenquotienten mittels Meta-Analysen zu berechnen.

Eine umfassende Literatursuche führte zu 56 Primärstudien, von denen 44 Studien in die meta-analytischen Untersuchungen eingeflossen sind. Da die Ergebnisse aus der Literatur sehr unterschiedlich und teilweise widersprüchlich sind, wurden mögliche konfundierende Einflussfaktoren wie Zugehörigkeit zu einer höheren taxonomischen Gruppe, Ausmaß genetischer Vielfalt der untersuchten Stichprobe sowie Messmethodik erhoben.

Die Ergebnisse zeugen von kleinen Geschlechtsunterschieden, mit Ausnahme des 4D:5D Verhältnisses für die vordere rechte Extremität und einigen zu mittleren Effektgrößen tendierenden Fingerlängenverhältnissen. Insgesamt tendieren die vorderen Extremitäten zu größeren Geschlechtsunterschieden. Außerdem weisen Fingerlängenverhältnisse, die den fünften Finger einbeziehen, größere Geschlechtsunterschiede auf.

Die Tiergruppen (Primaten, Nagetiere, Vögel, Reptilien und Amphibien) unterscheiden sich im Ausmaß der Geschlechtsunterschiede, wenn auch nicht signifikant. Reptilien und Amphibien tendieren zu größeren Geschlechtsunterschieden, während Primaten die kleinsten Unterschiede zeigen.

Darüber hinaus gibt es Hinweise, dass die genetische Diversität der untersuchten Tier-Stichprobe ebenfalls relevant ist. Genetisch idente Tiere weisen die kleinsten Geschlechtsunterschiede auf. Zudem wird deutlich, dass das Fingerlängenverhältnis/Digit Ratio eine starke erbliche Komponente besitzt.

Erheblichen Einfluss hat auch die Vorgangsweise bei der Messung der Fingerlängen. Messungen mittels digitaler Techniken sowie Messungen mithilfe eines Messschiebers oder Lineals, zumindest im

unbewegten Zustand des untersuchten Tieres, sind geeigneter als Messungen mittels Osteometrie, Röntgen oder indirekte Messungen von Abdrücken der Extremitäten.

Da sich die untersuchten Tierarten bedeutend hinsichtlich phylogenetischer und ontogenetischer Eigenschaften unterscheiden und deshalb zu sehr heterogenen Ergebnissen führen, scheint die Anwendung der Forschungserkenntnisse auf den Menschen nur bedingt möglich. Die genauen zeitlichen Muster und Vorgänge der Fingerausprägung, das Ausmaß und die Zeitpunkte der hormonellen Beeinflussung sowie die Sensitivität der Gewebeanlagen gegenüber diesen Hormonen unterscheiden sich beträchtlich zwischen den verschiedenen Arten.

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7. Appendices

7.1. Appendix A

7.1.1. Data extraction sheet

Report characteristics (R = Report)
R1. Report ID number
R2. First authors name
R3. Year of appearance of report or publication
R4. Type of report 1 = Journal article 2 = Book or book chapter 3 = Dissertation 4 = MA thesis 5 = Conference paper 6 = other
Setting Characteristics (S = Setting)
S1. Continent where study was conducted
S2. Country where study was conducted
Participant and sample characteristics (P = Participants)
P1. Examined animal group 1 = rodent 2 = primate 3 = bird 4 = reptile 5 = amphibian
P2. Examined animal species
P3. Age of examined animals 1 = Fetus

2 = Weanling 3 = Adolescent 4 = Adult
P4. Sample size (total)
P4. Sample size females
P5. Sample size males
P6. Weight P6a. Mean weight of females P6b. Mean weight of males
P7. Size P7a. Mean size of females P7b. Mean size of males
P8. Origin of examined animals 1 = Wild type, caught for examination 2 = Wild type but living in captivity 3 = Born and living in captivity 4 = Inbred 5 = Selective breeding
P9. Measurement material 1 = Living 2 = Dead and/or amputated 3 = Preserved (with soft tissue) 4 = skeleton (without soft tissue)
Outcome Measure (m = Measurement)
M1. Measurement procedure 1 = Directly (by ruler or (digital) calipers) 2 = Directly (osteometry) 3 = Indirectly (pins or stamps) 4 = Indirectly (digital photographs or scans)

5 = Indirectly (X-rays)
M2. Accuracy of measurement
M3. How many raters M3a. If more than one rater, information about inter-rater-reliability
M4. How many measurements per digit M4a. If more than one measurement, information about repeatability
M5. Rater blind to sex?
M6. Rater blind to side?
Results for comparisons of two groups (RM = Results for Comparisons of Means)
RM1. M for females
RM2. SD for females
RM3: SE for females
RM4. M for males
RM5. SD for males
RM6. SE for males
RM7. T-value
RM8. F-value
RM9. P-value
RM10. Cohen's d
RM11. Other statistics

7.2. Appendix B

7.2.1. Lists of included studies – 2D:4D

Table 14: List of studies included into meta-analyses – FR 2D:4D

Studies preceded by an asterisk (*) used pooled data for body sides and were included into the meta-analyses for both body sides each.

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	47	41	0.151	0.214	Primate
McMechan	2004	20	22	0.689	0.325	Rodent
Roney	2004	11	20	0.965	0.395	Primate
Rubolini (1)	2006	18	18	0.880	0.349	Reptile
Rubolini (2)	2006	17	11	0.890	0.405	Reptile
Chang	2006	61	87	0.164	0.167	Reptile
Manno	2008	39	39	0.126	0.227	Rodent
Lombardo	2008	25	25	0.370	0.285	Reptile
Lilley (1)	2009	47	60	0.279	0.196	Rodent
Lilley (2)	2009	9	25	0.060	0.389	Rodent
Yan	2009	116	158	0.083	0.122	Rodent
McIntyre	2009	66	52	0.436	0.188	Primate
***Nelson (1)**	2010	101	88	0.029	0.146	Primate
***Nelson (2)**	2010	300	597	0.160	0.071	Primate
Nelson	2010	17	8	0.270	0.430	Primate
Gomes	2011	218	229	0.149	0.095	Reptile
Direnzo (1)	2012	36	48	0.697	0.227	Amphibian
Direnzo (2)	2012	30	40	0.117	0.214	Amphibian
Direnzo (3)	2012	42	41	0.425	0.222	Reptile
Direnzo (4)	2012	40	34	0.412	0.236	Reptile
Abbott	2012	9	19	0.383	0.408	Primate
Auger	2013	20	20	1.555	0.303	Rodent
Zhao	2014	24	20	0.114	0.303	Rodent
Kaczmarski (1)	2015	42	36	0.765	0.235	Amphibian
Kaczmarski (2)	2015	41	32	0.196	0.236	Amphibian
Kaczmarski (3)	2015	31	28	0.192	0.261	Amphibian
Kaczmarski (4)	2015	19	17	0.597	0.341	Amphibian
Van Damme	2015	570	455	0.220	0.063	Reptile
Balogova	2015	32	30	0.096	0.254	Amphibian

Table 15: List of studies included into meta-analyses – FL 2D:4D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	47	41	0.317	0.215	Primate
Rubolini (1)	2006	18	18	1.060	0.356	Reptile
Rubolini (2)	2006	17	11	0.290	0.389	Reptile

Chang	2006	61	87	0.313	0.168	Reptile
Manno	2008	39	39	0.215	0.227	Rodent
Lombardo	2008	25	25	0.200	0.284	Reptile
Lilley (1)	2009	46	58	0.141	0.198	Rodent
Lilley (2)	2009	7	15	0.128	0.458	Rodent
Yan	2009	116	158	0.125	0.122	Rodent
McIntyre	2009	66	52	0.381	0.187	Primate
***Nelson (1)**	2010	101	88	0.029	0.146	Primate
***Nelson (2)**	2010	300	597	0.160	0.071	Primate
Nelson	2010	17	8	0.450	0.433	Primate
Gomes	2011	218	229	0.149	0.095	Reptile
Direnzo (1)	2012	35	48	0.932	0.234	Amphibian
Direnzo (2)	2012	30	38	0.618	0.250	Amphibian
Direnzo (3)	2012	41	41	0.746	0.228	Reptile
Direnzo (4)	2012	40	37	0.278	0.229	Reptile
Abbott	2012	9	19	0.264	0.406	Primate
Auger	2013	20	20	1.176	0.342	Rodent
Zhao	2014	24	20	0.024	0.303	Rodent
Kaczmarski (1)	2015	41	38	0.750	0.233	Amphibian
Kaczmarski (2)	2015	39	33	0.160	0.237	Amphibian
Kaczmarski (3)	2015	33	25	0.444	0.268	Amphibian
Kaczmarski (4)	2015	19	18	0.272	0.330	Amphibian
Van Damme	2015	570	455	0.275	0.063	Reptile
Balogova	2015	30	30	0.109	0.258	Amphibian

Table 16: List of studies included into meta-analysis – HR 2D:4D

Study	Year	N ♂	N ♀	d	SE	Animal group
Brown (1)	2002	15	17	0.807	0.368	Rodent
Brown (2)	2002	20	19	0.723	0.331	Rodent
McFadden	2003	48	42	0.015	0.211	Primate
Manning	2003	70	41	0.376	0.198	Rodent
Burley	2003	47	56	0.694	0.204	Bird
Bailey	2004	93	92	0.039	0.147	Rodent
Leoni	2005	16	26	0.599	0.324	Rodent
Forstmeier	2005	258	242	0.094	0.090	Bird
Chang	2006	61	87	0.704	0.172	Reptile
Navarro	2007	49	20	0.137	0.266	Bird

Saino	2007	50	62	0.626	0.195	Bird
Dreiss	2007	44	41	0.093	0.217	Bird
Erhan (1)	2007	44	44	0.084	0.213	Rodent
Erhan (2)	2007	10	14	0.211	0.415	Rodent
Erhan (3)	2007	24	23	0.124	0.292	Rodent
Manno	2008	39	39	0.066	0.227	Rodent
Hurd	2008	44	51	0.574	0.210	Rodent
Lombardo	2008	25	25	0.314	0.285	Reptile
Lombardo (1)	2008	58	62	0.259	0.183	Bird
Lombardo (2)	2008	33	38	0.405	0.240	Bird
Lombardo (3)	2008	10	19	0.039	0.391	Bird
Lombardo (4)	2008	12	12	0.127	0.409	Bird
***Leoni**	2008	30	35	0.668	0.256	Bird
Yan	2008	164	220	0.132	0.103	Rodent
Forstmeier	2008	22	26	0.100	0.290	Bird
Bogdan	2009	65	56	0.235	0.183	Bird
Ruuskanen	2011	182	198	0.032	0.103	Bird
Gomes	2011	229	229	0.195	0.094	Reptile
Zheng	2011	30	28	0.571	0.268	Rodent
Gooderham	2012	12	17	0.426	0.381	Rodent
Direnzo (1)	2012	35	47	0.199	0.224	Amphibian
Direnzo (2)	2012	31	36	0.096	0.245	Amphibian
Direnzo (3)	2012	40	41	0.565	0.227	Reptile
Direnzo (4)	2012	38	33	0.074	0.238	Reptile
Abbott	2012	9	33	0.191	0.377	Primate
Zhao	2014	39	37	0.215	0.304	Rodent
Kaczmarski (1)	2015	39	37	0.235	0.230	Amphibian
Kaczmarski (2)	2015	42	31	0.459	0.240	Amphibian
Kaczmarski (3)	2015	32	33	0.543	0.253	Amphibian
Kaczmarski (4)	2015	18	18	0.090	0.334	Amphibian
Van Damme	2015	570	455	0.523	0.064	Reptile
Balogova	2015	27	34	0.074	0.258	Amphibian

Table 17: List of studies included into meta-analysis – HL 2D:4D

Study	Year	N ♂	N ♀	d	SE	Animal group
Brown (1)	2002	15	17	0.054	0.354	Rodent
Brown (2)	2002	20	19	0.203	0.321	Rodent

McFadden	2003	48	42	0.107	0.211	Primate
Manning	2003	70	41	0.875	0.205	Rodent
Bailey	2005	92	92	0.230	0.148	Rodent
Leoni	2005	16	26	0.667	0.326	Rodent
Chang	2006	61	87	0.309	0.168	Reptile
Navarro	2007	49	20	0.159	0.266	Bird
Dreiss	2007	42	44	0.026	0.216	Bird
Manno	2008	39	39	0.123	0.227	Rodent
Erhan (1)	2007	44	44	0.200	0.214	Rodent
Erhan (2)	2007	10	14	0.358	0.417	Rodent
Erhan (3)	2007	24	23	0.035	0.292	Rodent
Manno	2008	39	39	0.123	0.227	Rodent
Lombardo	2008	25	25	0.345	0.285	Reptile
Lombardo (1)	2008	57	62	0.224	0.184	Bird
Lombardo (2)	2008	32	38	0.041	0.240	Bird
Lombardo (3)	2008	12	15	0.627	0.397	Bird
Lombardo (4)	2008	12	12	0.347	0.411	Bird
***Leoni**	2008	30	35	0.668	0.256	Bird
Yan	2008	208	220	0.128	0.097	Rodent
Chang	2008	40	44	0.643	0.224	Amphibian
Yan	2009	116	158	0.007	0.122	Rodent
Bogdan	2009	65	56	0.235	0.183	Bird
Gooderham	2012	12	17	0.200	0.378	Rodent
Direnzo (1)	2012	36	48	0.074	0.221	Amphibian
Direnzo (2)	2012	46	42	0.327	0.215	Amphibian
Direnzo (3)	2012	40	41	0.632	0.228	Reptile
Direnzo (4)	2012	39	32	0.162	0.239	Reptile
Abbott	2012	9	33	0.440	0.379	Primate
Zhao	2014	24	20	0.269	0.304	Rodent
Kaczmarski (1)	2015	40	38	0.593	0.231	Amphibian
Kaczmarski (2)	2015	41	33	0.424	0.236	Amphibian
Kaczmarski (3)	2015	34	33	0.845	0.255	Amphibian
Kaczmarski (4)	2015	18	16	0.471	0.348	Amphibian
Van Damme	2015	570	455	0.472	0.064	Reptile
Balogova	2015	28	27	0.043	0.270	Amphibian

7.2.2. *Lists of included studies – 2D:3D*

Table 18: List of studies included into meta-analysis – FR 2D:3D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	41	0.225	0.213	Primate
McMechan	2004	20	20	0.789	0.328	Rodent
Roney	2004	11	20	0.243	0.377	Primate
Rubolini (1)	2006	18	18	0.570	0.340	Reptile
Rubolini (2)	2006	17	11	0.890	0.405	Reptile
Manno	2008	39	39	0.050	0.226	Rodent
Lombardo	2008	25	25	0.820	0.294	Reptile
Auger	2013	20	20	0.571	0.323	Rodent
Balogova	2015	32	30	0.318	0.256	Amphibian
Van Damme	2015	570	455	0.220	0.063	Reptile

Table 19: List of studies included into meta-analysis – FL 2D:3D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	41	0.030	0.213	Primate
McMechan	2004	20	20	0.149	0.317	Rodent
Rubolini (1)	2006	18	18	0.890	0.349	Reptile
Rubolini (2)	2006	17	11	1.090	0.413	Reptile
Manno	2008	39	39	0.011	0.226	Rodent
Lombardo	2008	25	25	0.037	0.283	Reptile
Auger	2013	20	20	0.618	0.324	Rodent
Balogova	2015	30	29	0.040	0.260	Amphibian
Van Damme	2015	570	455	0.336	0.063	Reptile

Table 20: List of studies included into meta-analysis – HR 2D:3D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	49	40	0.337	0.215	Primate
Manning	2003	70	41	0.149	0.197	Rodent
Leoni	2005	16	26	0.887	0.332	Rodent
Saino	2007	18	30	0.142	0.298	Bird
Manno	2008	39	39	0.029	0.226	Rodent

Lombardo	2008	25	25	0.187	0.283	Reptile
***Leoni**	2008	30	35	0.506	0.253	Bird
Bogdan	2009	65	56	0.235	0.183	Bird
Ruuskanen	2011	172	190	0.254	0.106	Bird
Balogova	2015	34	27	0.088	0.259	Amphibian
Van Damme	2015	570	455	0.287	0.063	Reptile

Table 21: List of studies included into meta-analysis – HL 2D:3D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	49	40	0.494	0.216	Primate
Manning	2003	70	41	0.637	0.201	Rodent
Leoni	2005	16	26	0.336	0.320	Rodent
Saino	2007	18	30	0.316	0.300	Bird
Manno	2008	39	39	0.172	0.277	Rodent
Lombardo	2008	25	25	0.129	0.283	Reptile
***Leoni**	2008	30	35	0.506	0.253	Bird
Balogova	2015	30	27	0.107	0.265	Amphibian
Van Damme	2015	570	455	0.214	0.063	Reptile

7.2.3. Lists of included studies – 2D:5D

Table 22: List of included studies into meta-analysis – FR 2D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	39	0.646	0.221	Primate
McMechan	2004	20	20	0.559	0.322	Rodent
Roney	2004	11	20	0.489	0.380	Primate
Manno	2008	39	39	0.206	0.277	Rodent
Lombardo	2008	25	25	0.060	0.283	Reptile
Auger	2013	20	20	0.016	0.316	Rodent

Table 23: List of included studies into meta-analysis – FL 2D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	39	0.646	0.221	Primate
McMechan	2004	20	20	0.559	0.322	Rodent
Roney	2004	11	20	0.489	0.380	Primate
Manno	2008	39	39	0.206	0.277	Rodent
Lombardo	2008	25	25	0.060	0.283	Reptile
Auger	2013	20	20	0.016	0.316	Rodent

Table 24: List of included studies into meta-analysis – HR 2D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	42	0.601	0.216	Primate
Manning	2003	70	41	0.021	0.197	Rodent
Leoni	2005	16	26	0.745	0.328	Rodent
Manno	2008	39	39	0.007	0.226	Rodent
Lombardo	2008	25	25	0.710	0.292	Reptile

Table 25: List of included studies into meta-analysis – HL 2D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	42	0.783	0.219	Primate
Manning	2003	70	41	0.411	0.199	Rodent
Leoni	2005	16	26	0.237	0.319	Rodent
Manno	2008	39	39	0.010	0.226	Rodent
Lombardo	2008	25	25	0.000	0.283	Reptile

7.2.4. Lists of included studies – 3D:4D

Table 26: List of included studies into meta-analysis – FR 3D:4D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	41	0.460	0.215	Primate
McMechan	2003	20	20	0.149	0.317	Rodent

Roney	2004	11	20	1.313	0.411	Primate
Rubolini (1)	2005	18	18	0.530	0.339	Reptile
Rubolini (2)	2005	17	11	0.206	0.227	Reptile
Manno	2008	39	39	0.206	0.227	Rodent
Lombardo	2008	25	25	0.020	0.283	Reptile
Auger	2013	20	20	1.310	0.348	Rodent
Balogova	2015	33	31	0.141	0.250	Amphibian
Van Damme	2015	570	455	0.124	0.063	Reptile

Table 27: List of included studies into meta-analysis – FL 3D:4D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	41	0.492	0.216	Primate
McMechan	2003	20	20	0.062	0.316	Rodent
Rubolini (1)	2005	18	18	0.210	0.334	Reptile
Rubolini (2)	2005	17	11	0.780	0.401	Reptile
Manno	2008	39	39	0.316	0.228	Rodent
Lombardo	2008	25	25	0.170	0.283	Reptile
Auger	2013	20	20	0.896	0.332	Rodent
Balogova	2015	30	28	0.212	0.264	Amphibian
Van Damme	2015	570	455	0.006	0.063	Reptile

Table 28: List of included studies into meta-analysis – HR 3D:4D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	40	0.354	0.216	Primate
Manning	2003	70	41	0.235	0.197	Rodent
Leoni	2005	16	25	0.162	0.318	Rodent
Saino	2007	30	18	0.906	0.312	Bird
Manno	2008	39	39	0.007	0.226	Rodent
Lombardo	2008	25	25	0.320	0.285	Reptile
***Leoni**	2008	30	35	0.202	0.249	Bird
Bogdan	2009	65	56	0.235	0.183	Bird
Ruuskanen	2011	172	190	0.000	0.105	Bird
Tobler	2011	74	59	0.442	0.177	Reptile
Balogova	2015	33	28	0.017	0.257	Amphibian

Van Damme	2015	570	455	0.264	0.063	Reptile

Table 29: List of included studies into meta-analysis – HL 3D:4D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	40	0.437	0.217	Primate
Manning	2003	70	41	0.250	0.197	Rodent
Leoni	2005	16	26	0.159	0.318	Rodent
Saino	2007	30	18	0.474	0.302	Bird
Manno	2008	39	39	0.010	0.226	Rodent
Lombardo	2008	25	25	0.510	0.287	Reptile
***Leoni**	2008	30	35	0.202	0.249	Bird
Tobler	2011	75	59	0.387	0.176	Reptile
Balogova	2015	31	29	0.060	0.258	Amphibian
Van Damme	2015	570	455	0.338	0.063	Reptile

7.2.5. Lists of included studies – 3D:5D

Table 30: List of included studies into meta-analysis – FR 3D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	49	39	0.937	0.226	Primate
McMechan	2004	20	20	0.360	0.319	Rodent
Roney	2004	11	20	0.340	0.378	Primate
Manno	2008	39	39	0.239	0.227	Rodent
Lombardo	2008	25	25	0.283	0.284	Reptile
Auger	2013	20	20	0.368	0.319	Rodent

Table 31: List of included studies into meta-analysis – FL 3D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	49	39	0.937	0.226	Primate
McMechan	2004	20	20	0.360	0.319	Rodent

Roney	2004	11	20	0.340	0.378	Primate
Manno	2008	39	39	0.239	0.227	Rodent
Lombardo	2008	25	25	0.283	0.284	Reptile
Auger	2013	20	20	0.368	0.319	Rodent

Table 32: List of included studies into meta-analysis – HR 3D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	40	0.390	0.216	Primate
Manning	2003	70	41	0.061	0.197	Rodent
Leoni	2005	16	26	0.257	0.319	Rodent
Lombardo	2008	25	25	0.648	0.290	Reptile
Manno	2008	39	39	0.029	0.226	Rodent

Table 33: List of included studies into meta-analysis – HL 3D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	40	0.531	0.218	Primate
Manning	2003	70	41	0.045	0.197	Rodent
Leoni	2005	16	26	0.254	0.319	Rodent
Lombardo	2008	25	25	0.215	0.284	Reptile
Manno	2008	39	39	0.104	0.227	Rodent

7.2.6. Lists of included studies – 4D:5D

Table 34: List of included studies into meta-analysis – FR 4D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	39	0.933	0.227	Primate
McMechan	2003	20	20	0.764	0.328	Rodent
Roney	2004	11	20	1.120	0.401	Primate
Manno	2008	39	39	0.421	0.229	Rodent
Lombardo	2008	25	25	0.170	0.283	Reptile
Auger	2013	20	20	1.097	0.339	Rodent

Table 35: List of included studies into meta-analysis – FL 4D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	48	39	0.619	0.221	Primate
McMechan	2003	20	20	0.518	0.321	Rodent
Manno	2008	39	39	0.257	0.227	Rodent
Lombardo	2008	25	25	0.034	0.283	Reptile
Auger	2013	20	20	0.284	0.318	Rodent

Table 36: List of included studies into meta-analysis – HR 4D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	47	42	0.760	0.220	Primate
Manning	2003	70	41	0.189	0.197	Rodent
Leoni	2005	16	26	0.273	0.319	Rodent
Manno	2008	39	39	0.069	0.227	Rodent
Lombardo	2008	25	25	0.659	0.290	Reptile

Table 37: List of included studies into meta-analysis – HL 4D:5D

Study	Year	N ♂	N ♀	d	SE	Animal group
McFadden	2003	47	42	0.844	0.222	Primate
Manning	2003	70	41	0.130	0.197	Rodent
Leoni	2005	16	26	0.006	0.318	Rodent
Manno	2008	39	39	0.132	0.227	Rodent
Lombardo	2008	25	25	0.585	0.289	Reptile

7.2.7. List of included studies – 1D-5D

Table 38: List of included studies into meta-analysis – including first digit (all extremities)

Study	Ratio	Year	N ♂	N ♀	d	SE	Animal group
	FR 1D:2D						

McFadden		2003	46	38	0.276	0.220	Primate
Manno		2008	39	39	0.542	0.231	Rodent
Lombardo		2008	25	25	0.256	0.284	Reptile
	FL 1D:2D						
McFadden		2003	46	38	0.516	0.223	Primate
Manno		2008	39	39	0.226	0.227	Rodent
Lombardo		2008	25	25	0.372	0.285	Reptile
	HR 1D:2D						
McFadden		2003	45	37	0.110	0.222	Primate
Manno		2008	39	39	0.245	0.227	Rodent
Lombardo		2008	25	25	0.326	0.285	Reptile
	HL 1D:2D						
McFadden		2003	45	37	0.086	0.222	Primate
Manno		2008	39	39	0.370	0.228	Rodent
Lombardo		2008	25	25	0.155	0.283	Reptile
	FR 1D:3D						
McFadden		2003	47	38	0.337	0.220	Primate
Manno		2008	39	39	0.505	0.230	Rodent
Lombardo		2008	25	25	0.596	0.289	Reptile
	FL 1D:3D						
McFadden		2003	47	38	0.400	0.220	Primate
Manno		2008	39	39	0.161	0.227	Rodent
Lombardo		2008	25	25	0.389	0.286	Reptile
	HR 1D:3D						
McFadden		2003	45	35	0.106	0.226	Primate
Manno		2008	39	39	0.223	0.227	Rodent
Lombardo		2008	25	25	0.188	0.283	Reptile
***Genovart**		2008	111	95	0.026	0.140	Bird
	HL 1D:3D						
McFadden		2003	45	35	0.212	0.226	Primate
Manno		2008	39	39	0.274	0.228	Rodent
Lombardo		2008	25	25	0.057	0.283	Reptile
***Genovart**		2008	111	95	0.026	0.140	Bird
	FR 1D:4D						
McFadden		2003	46	38	0.166	0.220	Primate
Manno		2008	39	39	0.539	0.231	Rodent
Lombardo		2008	25	25	0.414	0.286	Reptile
	FL 1D:4D						
McFadden		2003	46	38	0.226	0.220	Primate

Manno		2008	39	39	0.029	0.226	Rodent
Lombardo		2008	25	25	0.431	0.286	Reptile
	HR 1D:4D						
McFadden		2003	44	37	0.066	0.223	Primate
Manno		2008	39	39	0.144	0.227	Rodent
Lombardo		2008	25	25	0.096	0.283	Reptile
	HL 1D:4D						
McFadden		2003	44	37	0.017	0.223	Primate
Manno		2008	39	39	0.260	0.227	Rodent
Lombardo		2008	25	25	0.217	0.284	Reptile
	FR 1D:5D						
McFadden		2003	47	36	0.267	0.222	Primate
Manno		2008	39	39	0.337	0.228	Rodent
Lombardo		2008	25	25	0.245	0.284	Reptile
	FL 1D:5D						
McFadden		2003	47	36	0.001	0.221	Primate
Manno		2008	39	39	0.337	0.337	Rodent
Lombardo		2008	25	25	0.450	0.450	Reptile
	HR 1D:5D						
McFadden		2003	44	37	0.323	0.224	Primate
Manno		2008	39	39	0.187	0.227	Rodent
Lombardo		2008	25	25	0.151	0.283	Reptile
	HL 1D:5D						
McFadden		2003	44	37	0.594	0.228	Primate
Manno		2008	39	39	0.298	0.228	Rodent
Lombardo		2008	25	25	0.062	0.283	Reptile

7.2.8. List of excluded studies from quantitative synthesis

Study	Exclusion Criteria
McFadden et al., 2005	No data for sex differences of digit ratios given
Romano et al., 2005	No data for sex differences of digit ratios given
Garamszegi et al., 2007	No data for sex differences of digit ratios given
Lilley et al., 2010	No data for control groups given
Nelson et al., 2010	No data for sex differences of digit ratios given

Forstmeier et al., 2010	No data for sex differences of digit ratios given
Nelson et al., 2011	Paleobiological study
Tobler et al., 2012	No data for sex differences of digit ratios given
Cain et al., 2012	No data for sex differences of digit ratios given
Howlett et al., 2012	No data for sex differences of digit ratios given
Fomina et al., 2012	No data for sex differences of digit ratios given
Howlett et al., 2013	No data for sex differences of digit ratios given
Burgess, 2015	No data for sex differences of digit ratios given
Olvera-Hernández et al., 2015	Study published after editorial deadline

7.3. Appendix C

7.3.1. Forest plots - 2D:4D

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,151	0,214	0,046	-0,268	0,570	0,706	0,480
McMechan, 2004	0,689	0,325	0,106	0,051	1,327	2,117	0,034
Roney, 2004	0,965	0,395	0,156	0,191	1,739	2,443	0,015
Rubolini, 2006 (1)	0,880	0,349	0,122	0,196	1,564	2,521	0,012
Rubolini, 2006 (2)	0,890	0,405	0,164	0,097	1,683	2,199	0,028
Chang, 2006	0,164	0,167	0,028	-0,163	0,492	0,983	0,325
Manno, 2008	0,126	0,227	0,051	-0,319	0,570	0,554	0,579
Lombardo, 2008	0,370	0,285	0,081	-0,189	0,929	1,297	0,195
Lilley, 2009 (1)	0,279	0,196	0,038	-0,105	0,663	1,425	0,154
Lilley, 2009 (2)	0,060	0,389	0,151	-0,702	0,822	0,154	0,878
Yan, 2009	0,083	0,122	0,015	-0,157	0,323	0,678	0,498
McIntyre, 2009	0,436	0,188	0,035	0,068	0,803	2,322	0,020
Nelson (1), 2010 (1)	0,029	0,146	0,021	-0,257	0,315	0,200	0,841
Nelson (1), 2010 (2)	0,160	0,071	0,005	0,021	0,299	2,255	0,024
Nelson (2), 2010	0,270	0,430	0,185	-0,574	1,114	0,627	0,530
Gomes, 2011	0,149	0,095	0,009	-0,036	0,335	1,577	0,115
Direnzo, 2012 (1)	0,697	0,227	0,052	0,252	1,142	3,071	0,002
Direnzo, 2012 (2)	0,117	0,242	0,058	-0,357	0,591	0,484	0,628
Abbott, 2012	0,383	0,408	0,166	-0,416	1,183	0,939	0,348
Auger, 2013	1,555	0,361	0,130	0,848	2,262	4,309	0,000
Zhao, 2014	0,114	0,303	0,092	-0,479	0,708	0,378	0,706
Kaczmarski, 2015 (1)	0,765	0,235	0,055	0,304	1,226	3,253	0,001
Kaczmarski, 2015 (2)	0,196	0,236	0,056	-0,267	0,660	0,830	0,407
Kaczmarski, 2015 (3)	0,192	0,261	0,068	-0,320	0,705	0,736	0,462
Kaczmarski, 2015 (4)	0,597	0,341	0,116	-0,072	1,266	1,750	0,080
Balogova, 2015	0,096	0,254	0,065	-0,403	0,594	0,377	0,706
Van Damme, 2015	0,220	0,063	0,004	0,097	0,344	3,497	0,000
Direnzo, 2012 (3)	0,425	0,222	0,049	-0,010	0,860	1,914	0,056
Direnzo, 2012 (4)	0,412	0,236	0,056	-0,050	0,874	1,748	0,080
	0,239	0,031	0,001	0,178	0,300	7,695	0,000

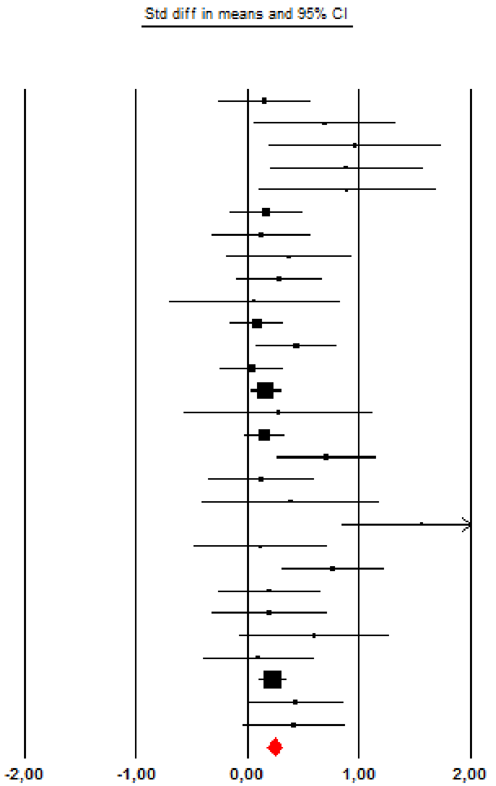

Figure 2: Forest plot for FR 2D:4D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
McFadden, 2003	0,241	0,031	0,001	0,179	0,303	7,674	0,000
McMechan, 2004	0,235	0,031	0,001	0,174	0,296	7,527	0,000
Roney, 2004	0,235	0,031	0,001	0,173	0,296	7,526	0,000
Rubolini, 2006 (1)	0,234	0,031	0,001	0,173	0,295	7,501	0,000
Rubolini, 2006 (2)	0,235	0,031	0,001	0,174	0,296	7,549	0,000
Chang, 2006	0,242	0,032	0,001	0,180	0,304	7,645	0,000
Manno, 2008	0,241	0,031	0,001	0,180	0,303	7,692	0,000
Lombardo, 2008	0,238	0,031	0,001	0,176	0,299	7,599	0,000
Lilley, 2009 (1)	0,238	0,031	0,001	0,176	0,300	7,565	0,000
Lilley, 2009 (2)	0,240	0,031	0,001	0,179	0,301	7,707	0,000
Yan, 2009	0,250	0,032	0,001	0,187	0,313	7,778	0,000
McIntyre, 2009	0,234	0,032	0,001	0,172	0,295	7,413	0,000
Nelson (1), 2010 (1)	0,249	0,032	0,001	0,187	0,311	7,832	0,000
Nelson (1), 2010 (2)	0,258	0,035	0,001	0,190	0,326	7,462	0,000
Nelson (2), 2010	0,239	0,031	0,001	0,178	0,300	7,670	0,000
Gomes, 2011	0,250	0,033	0,001	0,185	0,314	7,598	0,000
Direnzo, 2012 (1)	0,230	0,031	0,001	0,169	0,292	7,344	0,000
Direnzo, 2012 (2)	0,241	0,031	0,001	0,180	0,303	7,697	0,000
Abbott, 2012	0,238	0,031	0,001	0,177	0,299	7,646	0,000
Auger, 2013	0,229	0,031	0,001	0,168	0,290	7,351	0,000
Zhao, 2014	0,240	0,031	0,001	0,179	0,302	7,697	0,000
Kaczmarski, 2015 (1)	0,230	0,031	0,001	0,168	0,291	7,330	0,000
Kaczmarski, 2015 (2)	0,240	0,031	0,001	0,178	0,301	7,652	0,000
Kaczmarski, 2015 (3)	0,240	0,031	0,001	0,178	0,301	7,662	0,000
Kaczmarski, 2015 (4)	0,236	0,031	0,001	0,175	0,297	7,567	0,000
Balogova, 2015	0,241	0,031	0,001	0,180	0,303	7,707	0,000
Van Damme, 2015	0,245	0,036	0,001	0,175	0,315	6,863	0,000
Direnzo, 2012 (3)	0,235	0,031	0,001	0,174	0,297	7,501	0,000
Direnzo, 2012 (4)	0,236	0,031	0,001	0,175	0,297	7,530	0,000
	0,239	0,031	0,001	0,178	0,300	7,695	0,000

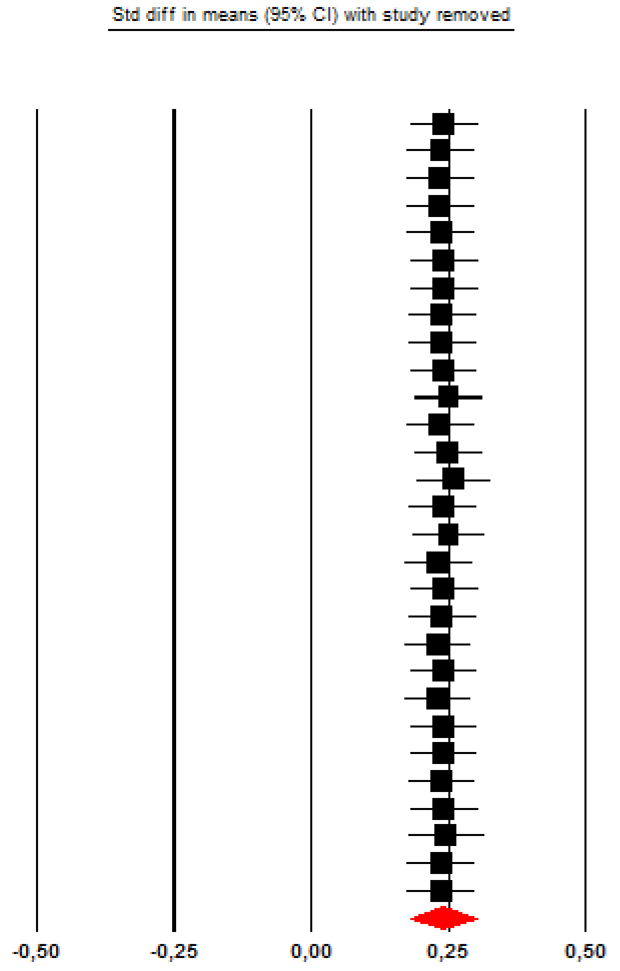

Figure 3: Sensitivity Analysis for FR 2D:4D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,317	0,215	0,046	-0,104	0,738	1,474	0,140
Rubolini, 2006 (1)	1,060	0,356	0,127	0,362	1,758	2,978	0,003
Rubolini, 2006 (2)	0,290	0,389	0,151	-0,472	1,052	0,746	0,456
Chang, 2006	0,313	0,168	0,028	-0,016	0,643	1,865	0,062
Manno, 2008	0,215	0,227	0,052	-0,230	0,660	0,947	0,344
Lombardo, 2008	0,200	0,284	0,080	-0,356	0,756	0,705	0,481
Lilley, 2009 (1)	0,141	0,198	0,039	-0,247	0,528	0,713	0,476
Lilley, 2009 (2)	0,128	0,458	0,210	-0,770	1,026	0,278	0,781
Yan, 2009	0,125	0,122	0,015	-0,115	0,364	1,018	0,309
McIntyre, 2009	0,381	0,187	0,035	0,015	0,748	2,039	0,041
Nelson (1), 2010 (1)	0,029	0,146	0,021	-0,257	0,315	0,200	0,841
Nelson (1), 2010 (2)	0,160	0,071	0,005	0,021	0,299	2,262	0,024
Nelson (2), 2010	0,450	0,433	0,188	-0,400	1,300	1,038	0,299
Gomes, 2011	0,149	0,095	0,009	-0,036	0,335	1,577	0,115
Direnzo, 2012 (1)	0,932	0,234	0,055	0,474	1,390	3,987	0,000
Direnzo, 2012 (2)	0,618	0,250	0,062	0,128	1,108	2,473	0,013
Abbott, 2012	0,264	0,406	0,165	-0,532	1,060	0,649	0,516
Auger, 2013	1,176	0,342	0,117	0,505	1,847	3,434	0,001
Zhao, 2014	0,024	0,303	0,092	-0,570	0,617	0,079	0,937
Kaczmarski, 2015 (1)	0,750	0,233	0,054	0,293	1,206	3,219	0,001
Kaczmarski, 2015 (2)	0,160	0,237	0,056	-0,305	0,624	0,674	0,501
Kaczmarski, 2015 (3)	0,444	0,268	0,072	-0,082	0,970	1,655	0,098
Kaczmarski, 2015 (4)	0,272	0,330	0,109	-0,376	0,920	0,823	0,411
Balogova, 2015	0,109	0,258	0,067	-0,397	0,615	0,422	0,673
Van Damme, 2015	0,275	0,063	0,004	0,152	0,399	4,361	0,000
Direnzo, 2012 (3)	0,746	0,228	0,052	0,298	1,194	3,266	0,001
Direnzo, 2012 (4)	0,278	0,229	0,053	-0,171	0,727	1,213	0,225
	0,261	0,031	0,001	0,200	0,323	8,321	0,000

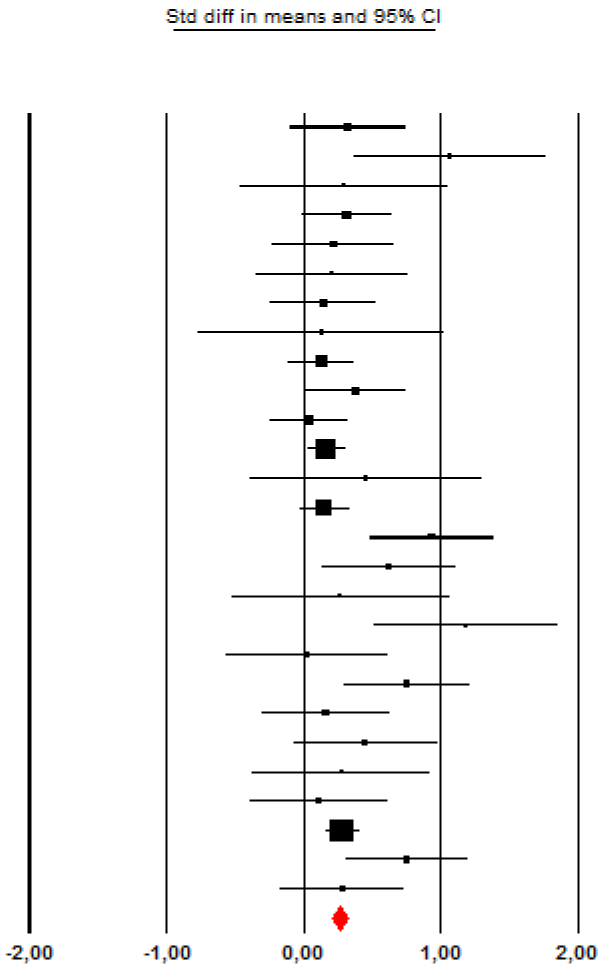

Figure 4: Forest plot for FL 2D:4D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,260	0,032	0,001	0,198	0,322	8,194	0,000
Rubolini, 2006 (1)	0,255	0,032	0,001	0,193	0,317	8,090	0,000
Rubolini, 2006 (2)	0,261	0,031	0,001	0,199	0,323	8,288	0,000
Chang, 2006	0,259	0,032	0,001	0,197	0,322	8,115	0,000
Manno, 2008	0,262	0,032	0,001	0,200	0,324	8,269	0,000
Lombardo, 2008	0,262	0,032	0,001	0,200	0,324	8,294	0,000
Lilley, 2009 (1)	0,264	0,032	0,001	0,202	0,327	8,313	0,000
Lilley, 2009 (2)	0,262	0,031	0,001	0,200	0,323	8,321	0,000
Yan, 2009	0,271	0,032	0,001	0,207	0,334	8,339	0,000
McIntyre, 2009	0,258	0,032	0,001	0,195	0,320	8,094	0,000
Nelson (1), 2010 (1)	0,272	0,032	0,001	0,209	0,335	8,477	0,000
Nelson (1), 2010 (2)	0,286	0,035	0,001	0,217	0,354	8,164	0,000
Nelson (2), 2010	0,260	0,031	0,001	0,199	0,322	8,268	0,000
Gomes, 2011	0,275	0,033	0,001	0,210	0,340	8,265	0,000
Direnzo, 2012 (1)	0,249	0,032	0,001	0,187	0,311	7,857	0,000
Direnzo, 2012 (2)	0,255	0,032	0,001	0,193	0,317	8,074	0,000
Abbott, 2012	0,261	0,031	0,001	0,199	0,323	8,296	0,000
Auger, 2013	0,253	0,032	0,001	0,192	0,315	8,040	0,000
Zhao, 2014	0,264	0,032	0,001	0,202	0,326	8,358	0,000
Kaczmarski, 2015 (1)	0,252	0,032	0,001	0,190	0,314	7,960	0,000
Kaczmarski, 2015 (2)	0,263	0,032	0,001	0,201	0,325	8,305	0,000
Kaczmarski, 2015 (3)	0,259	0,032	0,001	0,197	0,321	8,184	0,000
Kaczmarski, 2015 (4)	0,261	0,032	0,001	0,199	0,323	8,280	0,000
Balogova, 2015	0,263	0,032	0,001	0,201	0,325	8,331	0,000
Van Damme, 2015	0,257	0,036	0,001	0,186	0,327	7,091	0,000
Direnzo, 2012 (3)	0,252	0,032	0,001	0,190	0,314	7,948	0,000
Direnzo, 2012 (4)	0,261	0,032	0,001	0,199	0,323	8,232	0,000
	0,261	0,031	0,001	0,200	0,323	8,321	0,000

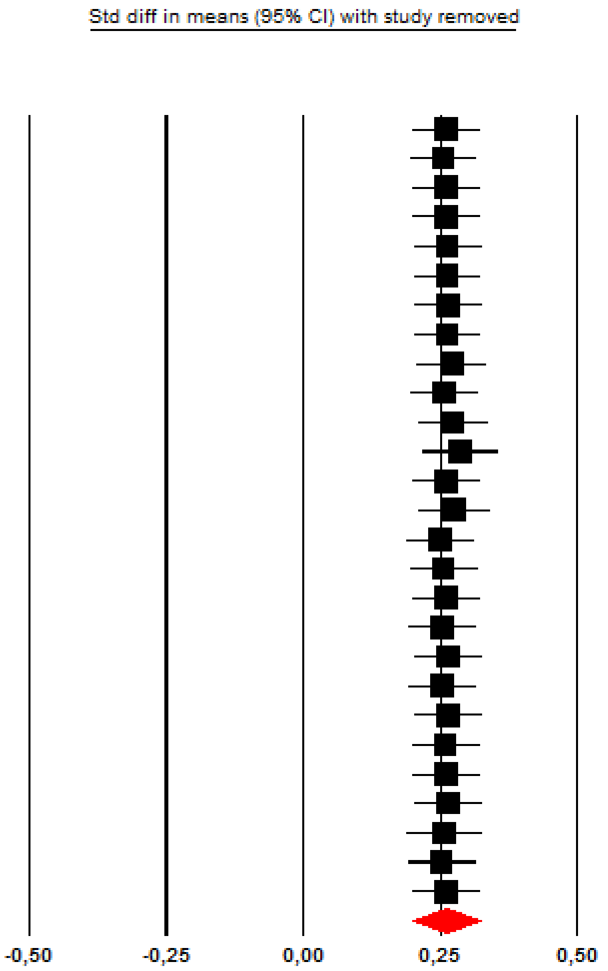

Figure 5: Sensitivity Analysis for FL 2D:4D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
Manning, 2003	0,376	0,198	0,039	-0,013	0,765	1,896	0,058
McFadden, 2003	0,015	0,211	0,045	-0,399	0,429	0,071	0,943
Burley,2003	0,694	0,204	0,041	0,295	1,093	3,409	0,001
Bailey, 2004	0,039	0,147	0,022	-0,249	0,327	0,265	0,791
Leoni, 2005	0,599	0,324	0,105	-0,037	1,234	1,845	0,065
Forstmeier, 2005	0,094	0,090	0,008	-0,082	0,269	1,047	0,295
Chang, 2006	0,704	0,172	0,030	0,367	1,041	4,097	0,000
Navarro, 2007	0,137	0,266	0,071	-0,384	0,658	0,516	0,606
Saino, 2007	0,626	0,195	0,038	0,244	1,007	3,214	0,001
Dreiss, 2007	0,093	0,217	0,047	-0,333	0,518	0,427	0,669
Manno, 2008	0,066	0,227	0,051	-0,378	0,510	0,292	0,770
Hurd, 2008	0,574	0,210	0,044	0,163	0,986	2,735	0,006
Lombardo, 2008	0,314	0,285	0,081	-0,244	0,872	1,103	0,270
Lombardo,2008 (1)	0,259	0,183	0,034	-0,100	0,619	1,414	0,157
Lombardo,2008 (2)	0,405	0,240	0,058	-0,067	0,876	1,683	0,092
Lombardo,2008 (3)	0,039	0,391	0,153	-0,727	0,805	0,100	0,920
Lombardo,2008 (4)	0,127	0,409	0,167	-0,674	0,928	0,310	0,757
Leoni, 2008	0,668	0,256	0,065	0,167	1,169	2,614	0,009
Yan, 2008	0,132	0,103	0,011	-0,071	0,334	1,275	0,202
Chang, 2008	0,771	0,226	0,051	0,327	1,215	3,405	0,001
Forstmeier, 2008	0,100	0,290	0,084	-0,468	0,668	0,346	0,730
Yan, 2009	0,057	0,122	0,015	-0,182	0,297	0,469	0,639
Forstmeier, 2010	0,033	0,059	0,003	-0,082	0,148	0,560	0,576
Bogdan, 2009	0,235	0,183	0,033	-0,124	0,594	1,284	0,199
Gooderham, 2012	0,426	0,381	0,145	-0,321	1,173	1,118	0,264
Ruuskanen,2011	0,032	0,103	0,011	-0,169	0,234	0,316	0,752
Gomes, 2011	0,195	0,094	0,009	0,011	0,379	2,081	0,037
Zheng, 2011	0,571	0,268	0,072	0,046	1,096	2,130	0,033
Direnzo, 2012 (1)	0,199	0,224	0,050	-0,240	0,637	0,888	0,375
Direnzo, 2012 (2)	0,096	0,245	0,060	-0,385	0,576	0,391	0,696
Direnzo, 2012 (3)	0,565	0,227	0,051	0,121	1,009	2,493	0,013
Direnzo, 2012 (4)	0,074	0,238	0,057	-0,393	0,541	0,311	0,756
Abbott, 2012	0,191	0,377	0,142	-0,547	0,930	0,508	0,611
Zhao, 2014	0,215	0,304	0,092	-0,380	0,810	0,708	0,479
Kaczmarski (1)	0,235	0,230	0,053	-0,217	0,686	1,019	0,308
Kaczmarski (2)	0,459	0,240	0,058	-0,011	0,929	1,915	0,055
Kaczmarski (3)	0,543	0,253	0,064	0,048	1,039	2,151	0,031
Kaczmarski (4)	0,090	0,334	0,111	-0,563	0,744	0,271	0,786
Brown, 2002 (1)	0,807	0,368	0,136	0,085	1,529	2,191	0,028
Brown, 2002 (2)	0,723	0,331	0,109	0,075	1,371	2,187	0,029
Balogova, 2015	0,074	0,258	0,066	-0,431	0,579	0,287	0,774
Van Damme, 2015	0,523	0,064	0,004	0,398	0,648	8,182	0,000
Erhan, 2007 (1)	0,084	0,213	0,045	-0,334	0,502	0,393	0,694
Erhan, 2007 (2)	0,211	0,415	0,172	-0,603	1,024	0,507	0,612
Erhan, 2007 (3)	0,124	0,292	0,085	-0,448	0,697	0,426	0,670
	0,279	0,041	0,002	0,199	0,359	6,863	0,000

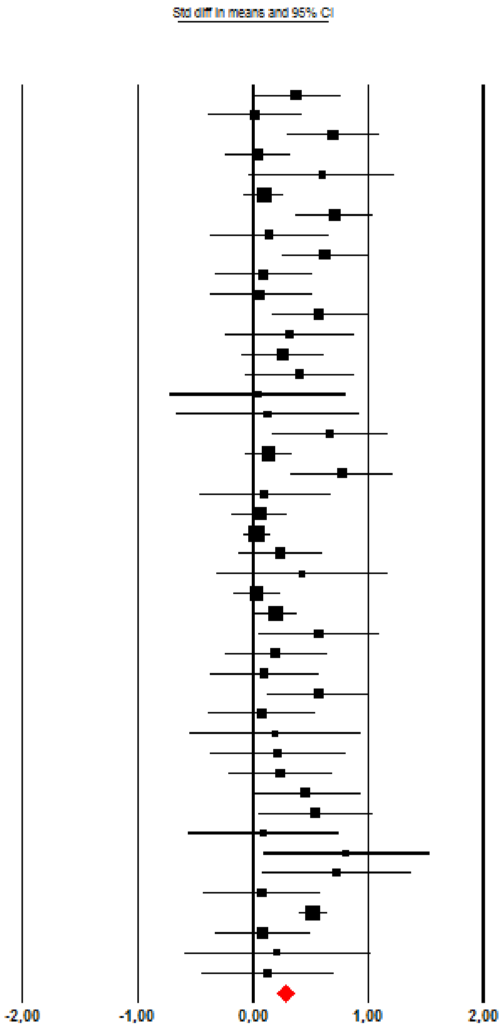

Figure 6: Forest plot for HR 2D:4D (Random-effects model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
Manning, 2003	0,277	0,041	0,002	0,196	0,358	6,683	0,000
McFadden, 2003	0,285	0,041	0,002	0,204	0,366	6,918	0,000
Burley,2003	0,268	0,040	0,002	0,189	0,347	6,634	0,000
Bailey, 2004	0,287	0,041	0,002	0,206	0,368	6,933	0,000
Leoni, 2005	0,275	0,041	0,002	0,195	0,355	6,721	0,000
Forstmeier, 2005	0,288	0,042	0,002	0,206	0,370	6,865	0,000
Chang, 2006	0,265	0,040	0,002	0,186	0,343	6,618	0,000
Navarro, 2007	0,282	0,041	0,002	0,201	0,363	6,827	0,000
Saino, 2007	0,269	0,041	0,002	0,190	0,349	6,625	0,000
Dreiss, 2007	0,283	0,041	0,002	0,202	0,365	6,855	0,000
Manno, 2008	0,284	0,041	0,002	0,203	0,365	6,872	0,000
Hurd, 2008	0,272	0,041	0,002	0,192	0,352	6,643	0,000
Lombardo, 2008	0,279	0,041	0,002	0,198	0,360	6,760	0,000
Lombardo,2008 (1)	0,280	0,042	0,002	0,199	0,362	6,730	0,000
Lombardo,2008 (2)	0,277	0,041	0,002	0,196	0,358	6,707	0,000
Lombardo,2008 (3)	0,281	0,041	0,002	0,201	0,362	6,859	0,000
Lombardo,2008 (4)	0,281	0,041	0,002	0,200	0,361	6,834	0,000
Leoni, 2008	0,272	0,041	0,002	0,192	0,351	6,672	0,000
Yan, 2008	0,286	0,042	0,002	0,204	0,369	6,796	0,000
Chang, 2008	0,267	0,040	0,002	0,189	0,346	6,656	0,000
Forstmeier, 2008	0,282	0,041	0,002	0,201	0,363	6,845	0,000
Yan, 2009	0,288	0,042	0,002	0,206	0,369	6,923	0,000
Forstmeier, 2010	0,290	0,040	0,002	0,212	0,368	7,280	0,000
Bogdan, 2009	0,281	0,042	0,002	0,199	0,362	6,746	0,000
Gooderham, 2012	0,278	0,041	0,002	0,197	0,358	6,768	0,000
Ruuskanen,2011	0,290	0,041	0,002	0,208	0,371	6,998	0,000
Gomes, 2011	0,284	0,042	0,002	0,201	0,367	6,685	0,000
Zheng, 2011	0,274	0,041	0,002	0,194	0,354	6,690	0,000
Direnzo, 2012 (1)	0,281	0,041	0,002	0,200	0,362	6,787	0,000
Direnzo, 2012 (2)	0,283	0,041	0,002	0,202	0,364	6,850	0,000
Direnzo, 2012 (3)	0,273	0,041	0,002	0,193	0,353	6,659	0,000
Direnzo, 2012 (4)	0,283	0,041	0,002	0,202	0,364	6,865	0,000
Abbott, 2012	0,280	0,041	0,002	0,200	0,361	6,816	0,000
Zhao, 2014	0,280	0,041	0,002	0,199	0,361	6,799	0,000
Kaczmarski (1)	0,280	0,041	0,002	0,199	0,362	6,770	0,000
Kaczmarski (2)	0,276	0,041	0,002	0,195	0,356	6,691	0,000
Kaczmarski (3)	0,274	0,041	0,002	0,194	0,355	6,683	0,000
Kaczmarski (4)	0,282	0,041	0,002	0,201	0,362	6,847	0,000
Brown, 2002 (1)	0,273	0,041	0,002	0,194	0,353	6,731	0,000
Brown, 2002 (2)	0,273	0,041	0,002	0,194	0,353	6,716	0,000
Balogova, 2015	0,283	0,041	0,002	0,202	0,364	6,862	0,000
Van Damme, 2015	0,255	0,038	0,001	0,182	0,329	6,802	0,000
Erhan, 2007 (1)	0,284	0,041	0,002	0,203	0,365	6,862	0,000
Erhan, 2007 (2)	0,280	0,041	0,002	0,199	0,360	6,815	0,000
Erhan, 2007 (3)	0,282	0,041	0,002	0,201	0,362	6,834	0,000
	0,279	0,041	0,002	0,199	0,359	6,863	0,000

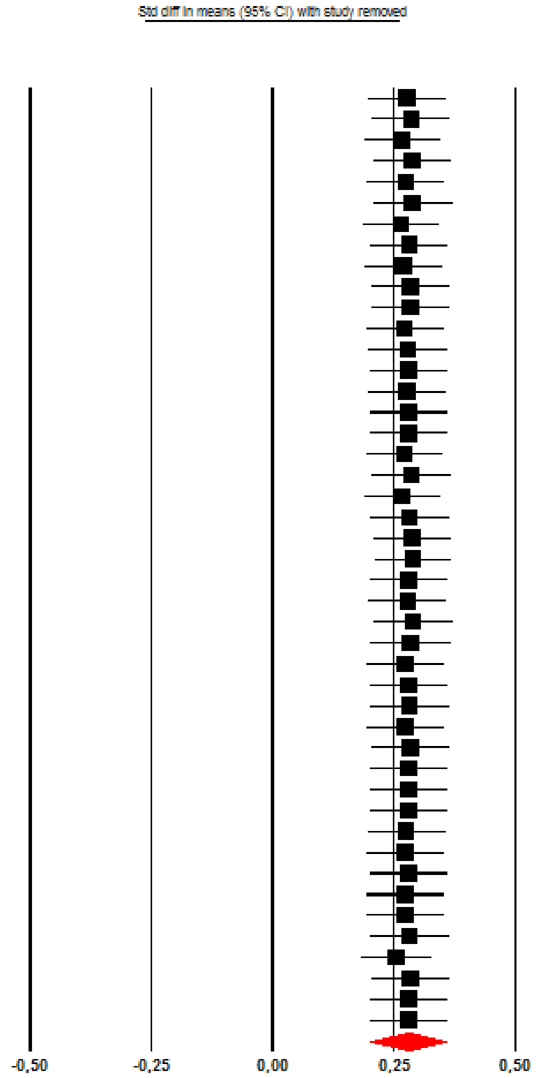

Figure 7: Sensitivity Analyses for HR 2D:4D (Random-effects model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,376	0,198	0,039	-0,013	0,765	1,896	0,058
McFadden, 2003	0,015	0,211	0,045	-0,399	0,429	0,071	0,943
Bailey, 2004	0,039	0,147	0,022	-0,249	0,327	0,265	0,791
Leoni, 2005	0,599	0,324	0,105	-0,037	1,234	1,845	0,065
Chang, 2006	0,704	0,172	0,030	0,367	1,041	4,097	0,000
Manno, 2008	0,066	0,227	0,051	-0,378	0,510	0,292	0,770
Hurd, 2008	0,574	0,210	0,044	0,163	0,986	2,735	0,006
Lombardo, 2008	0,314	0,285	0,081	-0,244	0,872	1,103	0,270
Yan, 2008	0,132	0,103	0,011	-0,071	0,334	1,275	0,202
Chang, 2008	0,771	0,226	0,051	0,327	1,215	3,405	0,001
Yan, 2009	0,057	0,122	0,015	-0,182	0,297	0,469	0,639
Gooderham, 2012	0,426	0,381	0,145	-0,321	1,173	1,118	0,264
Gomes, 2011	0,195	0,094	0,009	0,011	0,379	2,081	0,037
Zheng, 2011	0,571	0,268	0,072	0,046	1,096	2,130	0,033
Direnzo, 2012 (1)	0,199	0,224	0,050	-0,240	0,637	0,888	0,375
Direnzo, 2012 (2)	0,096	0,245	0,060	-0,385	0,576	0,391	0,696
Direnzo, 2012 (3)	0,565	0,227	0,051	0,121	1,009	2,493	0,013
Direnzo, 2012 (4)	0,074	0,238	0,057	-0,393	0,541	0,311	0,756
Abbott, 2012	0,191	0,377	0,142	-0,547	0,930	0,508	0,611
Zhao, 2014	0,215	0,304	0,092	-0,380	0,810	0,708	0,479
Kaczmarski (1)	0,235	0,230	0,053	-0,217	0,686	1,019	0,308
Kaczmarski (2)	0,459	0,240	0,058	-0,011	0,929	1,915	0,055
Kaczmarski (3)	0,543	0,253	0,064	0,048	1,039	2,151	0,031
Kaczmarski (4)	0,090	0,334	0,111	-0,563	0,744	0,271	0,786
Brown, 2002 (1)	0,807	0,368	0,136	0,085	1,529	2,191	0,028
Brown, 2002 (2)	0,723	0,331	0,109	0,075	1,371	2,187	0,029
Balogova, 2015	0,074	0,258	0,066	-0,431	0,579	0,287	0,774
Van Damme, 2015	0,523	0,064	0,004	0,398	0,648	8,182	0,000
Erhan, 2007 (1)	0,084	0,213	0,045	-0,334	0,502	0,393	0,694
Erhan, 2007 (2)	0,211	0,415	0,172	-0,603	1,024	0,507	0,612
Erhan, 2007 (3)	0,124	0,292	0,085	-0,448	0,697	0,426	0,670
	0,321	0,032	0,001	0,258	0,384	10,030	0,000

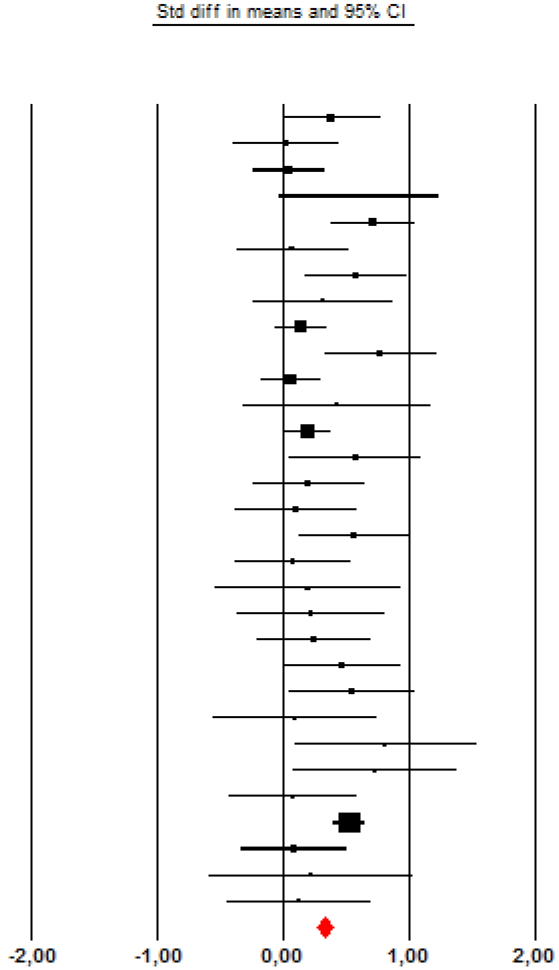

Figure 8: Forest plot for HR 2D:4D without bird data (Fixed-effect model)

Study name	Statistics for each study							Std diff in means and 95% CI
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
Brown, 2002 (1)	0,054	0,354	0,126	-0,640	0,748	0,152	0,879	
Brown, 2002 (2)	0,203	0,321	0,103	-0,426	0,833	0,632	0,527	
Manning, 2003	0,875	0,205	0,042	0,473	1,277	4,264	0,000	
Bailey, 2005	0,230	0,148	0,022	-0,060	0,520	1,555	0,120	
Leoni, 2005	0,667	0,326	0,106	0,028	1,306	2,047	0,041	
Chang, 2006	0,309	0,168	0,028	-0,020	0,638	1,839	0,066	
Navarro, 2007	0,159	0,266	0,071	-0,362	0,679	0,597	0,550	
Saino, 2007	0,154	0,190	0,036	-0,219	0,527	0,809	0,419	
Dreiss, 2007	0,026	0,216	0,047	-0,396	0,449	0,123	0,902	
Manno, 2008	0,123	0,227	0,051	-0,321	0,567	0,542	0,587	
Lombardo (1), 2008	0,345	0,285	0,081	-0,213	0,904	1,212	0,225	
Lombardo (2), 2008 (1)	0,224	0,184	0,034	-0,137	0,585	1,216	0,224	
Lombardo (2), 2008 (2)	0,041	0,240	0,058	-0,430	0,511	0,170	0,865	
Lombardo (2), 2008 (3)	0,627	0,397	0,157	-0,150	1,405	1,582	0,114	
Lombardo (2), 2008 (4)	0,347	0,411	0,169	-0,459	1,153	0,844	0,399	
Leoni, 2008	0,668	0,256	0,065	0,167	1,169	2,614	0,009	
Yan, 2008	0,128	0,097	0,009	-0,062	0,318	1,325	0,185	
Chang, 2008	0,643	0,224	0,050	0,204	1,082	2,870	0,004	
Yan, 2009	0,007	0,122	0,015	-0,233	0,246	0,056	0,955	
McFadden, 2003	0,107	0,211	0,045	-0,307	0,521	0,506	0,613	
Bogdan, 2009	0,235	0,183	0,033	-0,124	0,594	1,284	0,199	
Gooderham, 2012	0,200	0,378	0,143	-0,541	0,941	0,529	0,597	
Direnzo, 2012 (1)	0,074	0,221	0,049	-0,358	0,506	0,336	0,737	
Direnzo, 2012 (2)	0,327	0,215	0,046	-0,094	0,748	1,522	0,128	
Direnzo, 2012 (3)	0,632	0,228	0,052	0,186	1,078	2,775	0,006	
Direnzo, 2012 (4)	0,162	0,239	0,057	-0,306	0,630	0,678	0,498	
Abbott, 2012	0,440	0,379	0,144	-0,303	1,183	1,160	0,246	
Zhao, 2014	0,269	0,304	0,092	-0,327	0,865	0,885	0,376	
Kaczmarski, 2015 (1)	0,593	0,231	0,054	0,139	1,047	2,562	0,010	
Kaczmarski, 2015 (2)	0,424	0,236	0,056	-0,039	0,888	1,794	0,073	
Kaczmarski, 2015 (3)	0,845	0,255	0,065	0,345	1,345	3,314	0,001	
Kaczmarski, 2015 (4)	0,471	0,348	0,121	-0,212	1,154	1,352	0,176	
Balogova, 2015	0,043	0,270	0,073	-0,485	0,572	0,161	0,872	
Van Damme, 2015	0,472	0,064	0,004	0,347	0,597	7,402	0,000	
Erhan, 2007 (1)	0,200	0,214	0,046	-0,219	0,619	0,937	0,349	
Erhan, 2007 (2)	0,358	0,417	0,174	-0,460	1,175	0,857	0,391	
Erhan, 2007 (3)	0,035	0,292	0,085	-0,537	0,607	0,121	0,903	
	0,311	0,031	0,001	0,250	0,373	9,900	0,000	

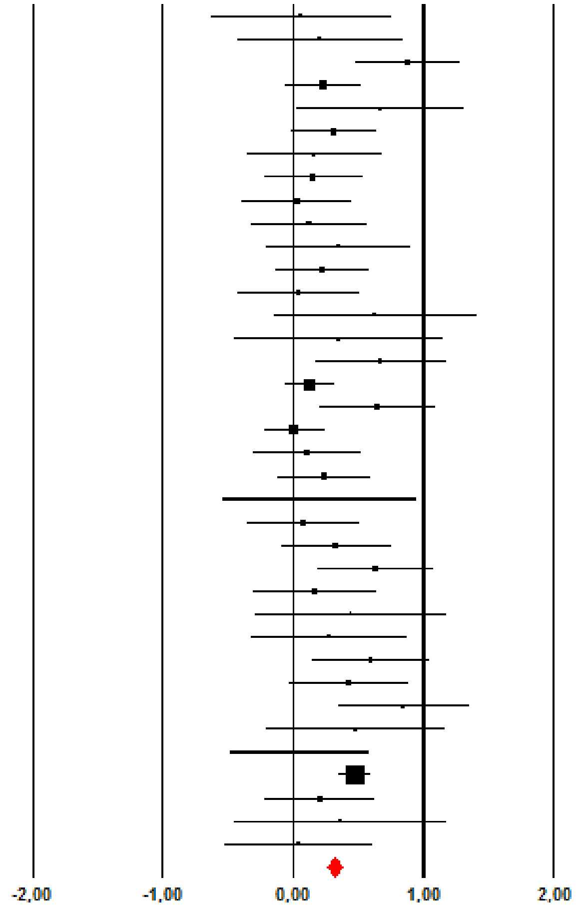

Figure 9: Forest plot for HL 2D:4D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
Brown, 2002 (1)	0,313	0,032	0,001	0,252	0,375	9,926	0,000
Brown, 2002 (2)	0,312	0,032	0,001	0,251	0,374	9,886	0,000
Manning, 2003	0,298	0,032	0,001	0,235	0,360	9,357	0,000
Bailey, 2005	0,315	0,032	0,001	0,252	0,378	9,794	0,000
Leoni, 2005	0,308	0,032	0,001	0,246	0,370	9,748	0,000
Chang, 2006	0,312	0,032	0,001	0,249	0,374	9,728	0,000
Navarro, 2007	0,314	0,032	0,001	0,252	0,376	9,899	0,000
Saino, 2007	0,316	0,032	0,001	0,253	0,378	9,903	0,000
Dreiss, 2007	0,318	0,032	0,001	0,255	0,380	9,969	0,000
Manno, 2008	0,315	0,032	0,001	0,253	0,377	9,921	0,000
Lombardo (1), 2008	0,311	0,032	0,001	0,249	0,373	9,827	0,000
Lombardo (2), 2008 (1)	0,314	0,032	0,001	0,251	0,377	9,837	0,000
Lombardo (2), 2008 (2)	0,316	0,032	0,001	0,254	0,378	9,964	0,000
Lombardo (2), 2008 (3)	0,309	0,032	0,001	0,248	0,371	9,806	0,000
Lombardo (2), 2008 (4)	0,311	0,032	0,001	0,249	0,373	9,865	0,000
Leoni, 2008	0,306	0,032	0,001	0,244	0,368	9,652	0,000
Yan, 2008	0,333	0,033	0,001	0,268	0,398	10,013	0,000
Chang, 2008	0,305	0,032	0,001	0,242	0,367	9,592	0,000
Yan, 2009	0,333	0,033	0,001	0,269	0,397	10,230	0,000
McFadden, 2003	0,316	0,032	0,001	0,254	0,378	9,936	0,000
Bogdan, 2009	0,314	0,032	0,001	0,251	0,376	9,826	0,000
Gooderham, 2012	0,312	0,032	0,001	0,250	0,374	9,891	0,000
Direnzo, 2012 (1)	0,316	0,032	0,001	0,254	0,379	9,954	0,000
Direnzo, 2012 (2)	0,311	0,032	0,001	0,249	0,373	9,783	0,000
Direnzo, 2012 (3)	0,305	0,032	0,001	0,243	0,367	9,609	0,000
Direnzo, 2012 (4)	0,314	0,032	0,001	0,252	0,376	9,897	0,000
Abbott, 2012	0,311	0,032	0,001	0,249	0,372	9,838	0,000
Zhao, 2014	0,312	0,032	0,001	0,250	0,374	9,862	0,000
Kaczmarski, 2015 (1)	0,306	0,032	0,001	0,244	0,368	9,642	0,000
Kaczmarski, 2015 (2)	0,309	0,032	0,001	0,247	0,372	9,748	0,000
Kaczmarski, 2015 (3)	0,303	0,032	0,001	0,241	0,365	9,565	0,000
Kaczmarski, 2015 (4)	0,310	0,032	0,001	0,248	0,372	9,818	0,000
Balogova, 2015	0,315	0,032	0,001	0,253	0,377	9,949	0,000
Van Damme, 2015	0,260	0,036	0,001	0,189	0,331	7,182	0,000
Erhan, 2007 (1)	0,314	0,032	0,001	0,252	0,376	9,870	0,000
Erhan, 2007 (2)	0,311	0,032	0,001	0,249	0,373	9,864	0,000
Erhan, 2007 (3)	0,315	0,032	0,001	0,253	0,377	9,945	0,000
	0,311	0,031	0,001	0,250	0,373	9,900	0,000

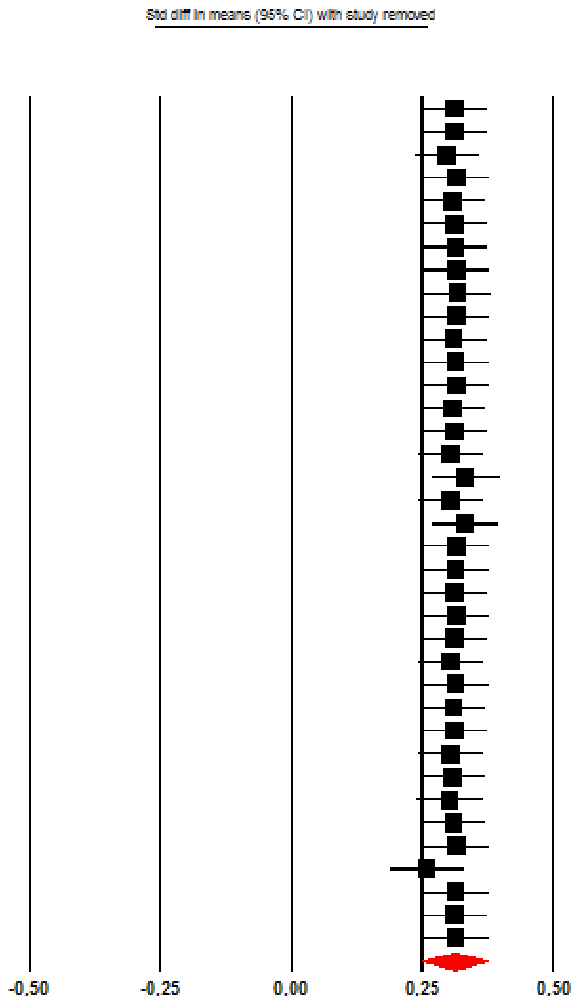

Figure 10: Sensitivity analysis for HL 2D:4D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Brown, 2002 (1)	0,054	0,354	0,126	-0,640	0,748	0,152	0,879
Brown, 2002 (2)	0,203	0,321	0,103	-0,426	0,833	0,632	0,527
Manning, 2003	0,875	0,205	0,042	0,473	1,277	4,264	0,000
Bailey, 2005	0,230	0,148	0,022	-0,060	0,520	1,555	0,120
Leoni, 2005	0,667	0,326	0,106	0,028	1,306	2,047	0,041
Chang, 2006	0,309	0,168	0,028	-0,020	0,638	1,839	0,066
Manno, 2008	0,123	0,227	0,051	-0,321	0,567	0,542	0,587
Lombardo (1), 2008	0,345	0,285	0,081	-0,213	0,904	1,212	0,225
Chang, 2008	0,643	0,224	0,050	0,204	1,082	2,870	0,004
Yan, 2009	0,007	0,122	0,015	-0,233	0,246	0,056	0,955
McFadden, 2003	0,107	0,211	0,045	-0,307	0,521	0,506	0,613
Gooderham, 2012	0,200	0,378	0,143	-0,541	0,941	0,529	0,597
Direnzo, 2012 (1)	0,074	0,221	0,049	-0,358	0,506	0,336	0,737
Direnzo, 2012 (2)	0,327	0,215	0,046	-0,094	0,748	1,522	0,128
Direnzo, 2012 (3)	0,632	0,228	0,052	0,186	1,078	2,775	0,006
Direnzo, 2012 (4)	0,162	0,239	0,057	-0,306	0,630	0,678	0,498
Abbott, 2012	0,440	0,379	0,144	-0,303	1,183	1,160	0,246
Zhao, 2014	0,269	0,304	0,092	-0,327	0,865	0,885	0,376
Kaczmarski, 2015 (1)	0,593	0,231	0,054	0,139	1,047	2,562	0,010
Kaczmarski, 2015 (2)	0,424	0,236	0,056	-0,039	0,888	1,794	0,073
Kaczmarski, 2015 (3)	0,845	0,255	0,065	0,345	1,345	3,314	0,001
Kaczmarski, 2015 (4)	0,471	0,348	0,121	-0,212	1,154	1,352	0,176
Balogova, 2015	0,043	0,270	0,073	-0,485	0,572	0,161	0,872
Van Damme, 2015	0,472	0,064	0,004	0,347	0,597	7,402	0,000
Erhan, 2007 (1)	0,200	0,214	0,046	-0,219	0,619	0,937	0,349
Erhan, 2007 (2)	0,358	0,417	0,174	-0,460	1,175	0,857	0,391
Erhan, 2007 (3)	0,035	0,292	0,085	-0,537	0,607	0,121	0,903
	0,358	0,037	0,001	0,285	0,430	9,706	0,000

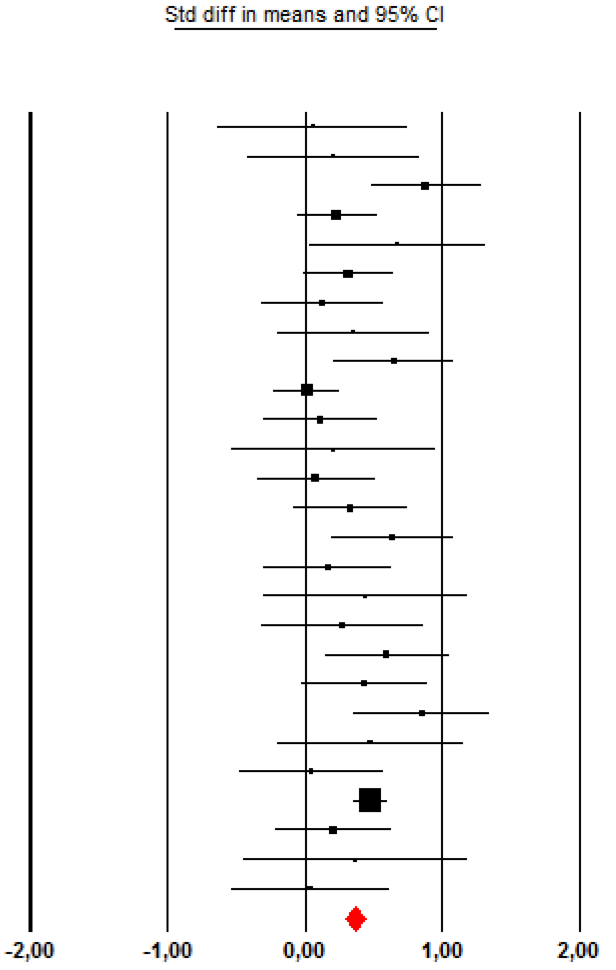

Figure 11: Forest plot for HL 2D:4D without bird data (Fixed-effect model)

7.3.2. Forest plots – 2D:3D

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
McFadden, 2003	0,225	0,213	0,046	-0,193	0,643	1,055	0,292
McMechan, 2004	0,789	0,328	0,108	0,146	1,432	2,403	0,016
Roney, 2004	0,243	0,377	0,142	-0,495	0,982	0,646	0,518
Rubolini, 2006 (1)	0,570	0,340	0,116	-0,096	1,236	1,676	0,094
Rubolini, 2006 (2)	0,890	0,405	0,164	0,097	1,683	2,199	0,028
Manno, 2008	0,050	0,226	0,051	-0,394	0,494	0,221	0,825
Lombardo, 2008	0,820	0,294	0,087	0,243	1,397	2,784	0,005
Auger, 2013	0,571	0,323	0,104	-0,061	1,204	1,771	0,077
Balogova, 2015	0,318	0,256	0,065	-0,183	0,819	1,243	0,214
Van Damme, 2015	0,220	0,063	0,004	0,097	0,344	3,497	0,000
	0,279	0,053	0,003	0,176	0,382	5,297	0,000

Std diff in means and 95% CI

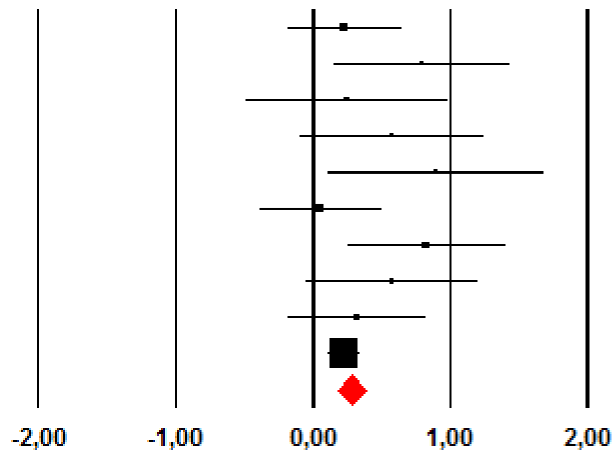

Figure12: Forest plot for FR 2D:3D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,282	0,054	0,003	0,176	0,389	5,198	0,000
McMechan, 2004	0,266	0,053	0,003	0,161	0,370	4,976	0,000
Roney, 2004	0,280	0,053	0,003	0,175	0,384	5,258	0,000
Rubolini, 2006 (1)	0,272	0,053	0,003	0,167	0,376	5,099	0,000
Rubolini, 2006 (2)	0,268	0,053	0,003	0,164	0,373	5,054	0,000
Manno, 2008	0,292	0,054	0,003	0,186	0,398	5,394	0,000
Lombardo, 2008	0,261	0,054	0,003	0,156	0,366	4,878	0,000
Auger, 2013	0,271	0,053	0,003	0,166	0,376	5,076	0,000
Balogova, 2015	0,277	0,054	0,003	0,172	0,383	5,152	0,000
Van Damme, 2015	0,414	0,096	0,009	0,226	0,602	4,322	0,000
	0,279	0,053	0,003	0,176	0,382	5,297	0,000

Std diff in means (95% CI) with study removed

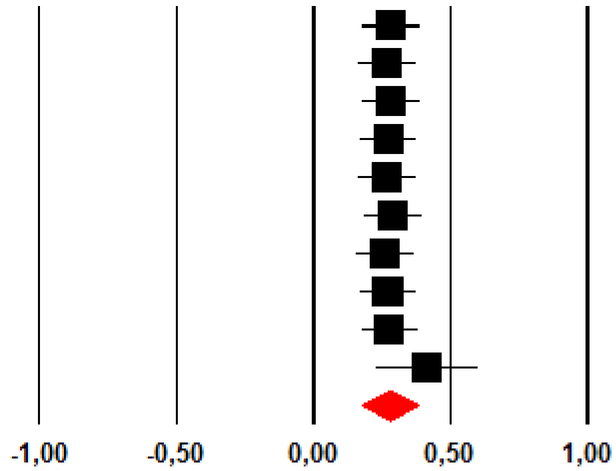

Figure 13: Sensitivity analysis for FR 2D:3D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
McFadden, 2003	0,030	0,213	0,045	-0,387	0,447	0,141	0,888
McMechan, 2004	0,149	0,317	0,100	-0,471	0,770	0,471	0,637
Rubolini, 2006 (1)	0,890	0,349	0,122	0,205	1,575	2,547	0,011
Rubolini, 2006 (2)	1,090	0,413	0,171	0,280	1,900	2,636	0,008
Manno, 2008	0,011	0,226	0,051	-0,433	0,454	0,047	0,963
Lombardo, 2008	0,037	0,283	0,080	-0,517	0,592	0,132	0,895
Auger, 2013	0,618	0,324	0,105	-0,016	1,253	1,910	0,056
Balogova, 2015	0,040	0,260	0,068	-0,470	0,551	0,155	0,877
Van Damme, 2015	0,336	0,063	0,004	0,212	0,460	5,302	0,000
	0,303	0,053	0,003	0,199	0,408	5,690	0,000

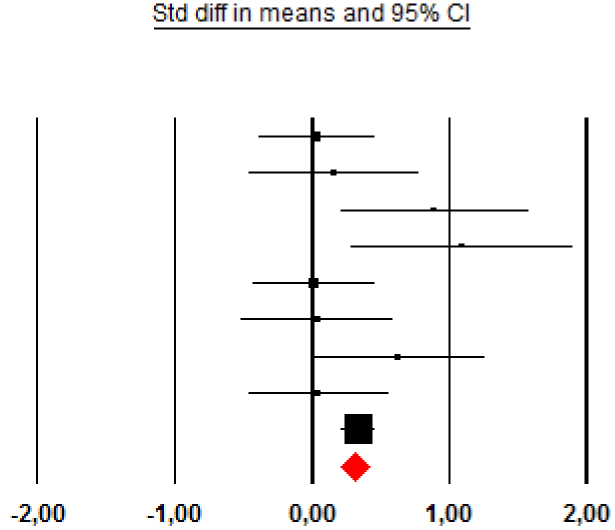

Figure 14: Forest plot for FL 2D:3D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,322	0,055	0,003	0,214	0,430	5,841	0,000
McMechan, 2004	0,308	0,054	0,003	0,202	0,414	5,692	0,000
Rubolini, 2006 (1)	0,289	0,054	0,003	0,184	0,395	5,364	0,000
Rubolini, 2006 (2)	0,290	0,054	0,003	0,185	0,395	5,395	0,000
Manno, 2008	0,320	0,055	0,003	0,213	0,428	5,843	0,000
Lombardo, 2008	0,313	0,054	0,003	0,207	0,419	5,769	0,000
Auger, 2013	0,295	0,054	0,003	0,189	0,400	5,450	0,000
Balogova, 2015	0,315	0,054	0,003	0,208	0,422	5,781	0,000
Van Damme, 2015	0,224	0,099	0,010	0,031	0,418	2,272	0,023
	0,303	0,053	0,003	0,199	0,408	5,690	0,000

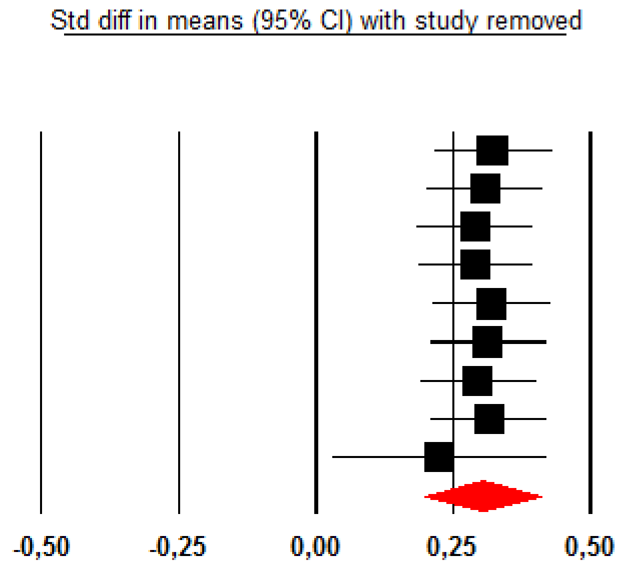

Figure 15: Sensitivity analysis for FL 2D:3D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,225	0,213	0,046	-0,193	0,643	1,055	0,292
McMechan, 2004	0,789	0,328	0,108	0,146	1,432	2,403	0,016
Roney, 2004	0,243	0,377	0,142	-0,495	0,982	0,646	0,518
Rubolini, 2006 (1)	0,570	0,340	0,116	-0,096	1,236	1,676	0,094
Rubolini, 2006 (2)	0,890	0,405	0,164	0,097	1,683	2,199	0,028
Manno, 2008	0,050	0,226	0,051	-0,394	0,494	0,221	0,825
Lombardo, 2008	0,820	0,294	0,087	0,243	1,397	2,784	0,005
Auger, 2013	0,571	0,323	0,104	-0,061	1,204	1,771	0,077
Balogova, 2015	0,318	0,256	0,065	-0,183	0,819	1,243	0,214
Van Damme, 2015	0,220	0,063	0,004	0,097	0,344	3,497	0,000
	0,279	0,053	0,003	0,176	0,382	5,297	0,000

Statistics for each study

Std diff in means and 95% CI

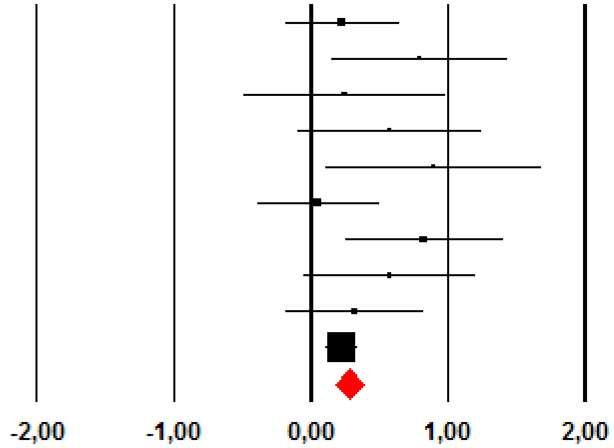

Figure 16: Forest plot for HR 2D:3D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
McFadden, 2003	0,282	0,054	0,003	0,176	0,389	5,198	0,000
McMechan, 2004	0,266	0,053	0,003	0,161	0,370	4,976	0,000
Roney, 2004	0,280	0,053	0,003	0,175	0,384	5,258	0,000
Rubolini, 2006 (1)	0,272	0,053	0,003	0,167	0,376	5,099	0,000
Rubolini, 2006 (2)	0,268	0,053	0,003	0,164	0,373	5,054	0,000
Manno, 2008	0,292	0,054	0,003	0,186	0,398	5,394	0,000
Lombardo, 2008	0,261	0,054	0,003	0,156	0,366	4,878	0,000
Auger, 2013	0,271	0,053	0,003	0,166	0,376	5,076	0,000
Balogova, 2015	0,277	0,054	0,003	0,172	0,383	5,152	0,000
Van Damme, 2015	0,414	0,096	0,009	0,226	0,602	4,322	0,000
	0,279	0,053	0,003	0,176	0,382	5,297	0,000

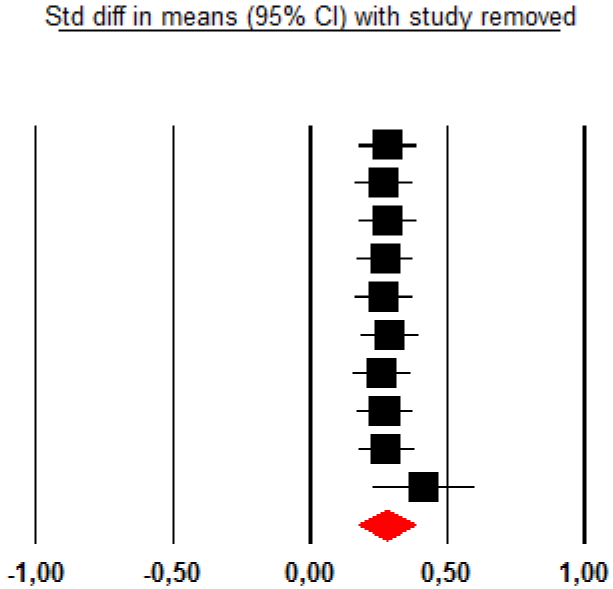

Figure 17: Sensitivity analysis for HR 2D:3D (Fixed-effect model)

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,030	0,213	0,045	-0,387	0,447	0,141	0,888
McMechan, 2004	0,149	0,317	0,100	-0,471	0,770	0,471	0,637
Rubolini, 2006 (1)	0,890	0,349	0,122	0,205	1,575	2,547	0,011
Rubolini, 2006 (2)	1,090	0,413	0,171	0,280	1,900	2,636	0,008
Manno, 2008	0,011	0,226	0,051	-0,433	0,454	0,047	0,963
Lombardo, 2008	0,037	0,283	0,080	-0,517	0,592	0,132	0,895
Auger, 2013	0,618	0,324	0,105	-0,016	1,253	1,910	0,056
Balogova, 2015	0,040	0,260	0,068	-0,470	0,551	0,155	0,877
Van Damme, 2015	0,336	0,063	0,004	0,212	0,460	5,302	0,000
	0,303	0,053	0,003	0,199	0,408	5,690	0,000

Std diff in means and 95% CI

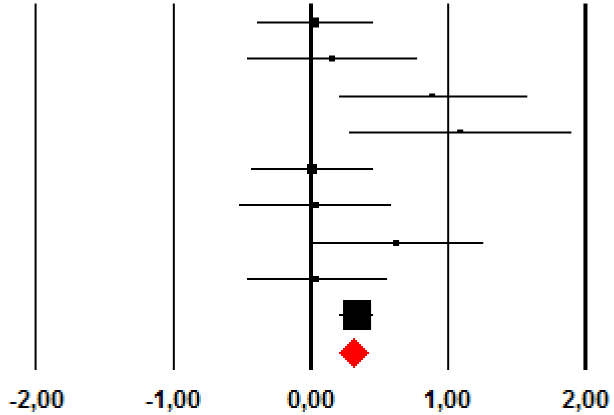

Figure 18: Forest plot for HL 2D:3D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,322	0,055	0,003	0,214	0,430	5,841	0,000
McMechan, 2004	0,308	0,054	0,003	0,202	0,414	5,692	0,000
Rubolini, 2006 (1)	0,289	0,054	0,003	0,184	0,395	5,364	0,000
Rubolini, 2006 (2)	0,290	0,054	0,003	0,185	0,395	5,395	0,000
Manno, 2008	0,320	0,055	0,003	0,213	0,428	5,843	0,000
Lombardo, 2008	0,313	0,054	0,003	0,207	0,419	5,769	0,000
Auger, 2013	0,295	0,054	0,003	0,189	0,400	5,450	0,000
Balogova, 2015	0,315	0,054	0,003	0,208	0,422	5,781	0,000
Van Damme, 2015	0,224	0,099	0,010	0,031	0,418	2,272	0,023
	0,303	0,053	0,003	0,199	0,408	5,690	0,000

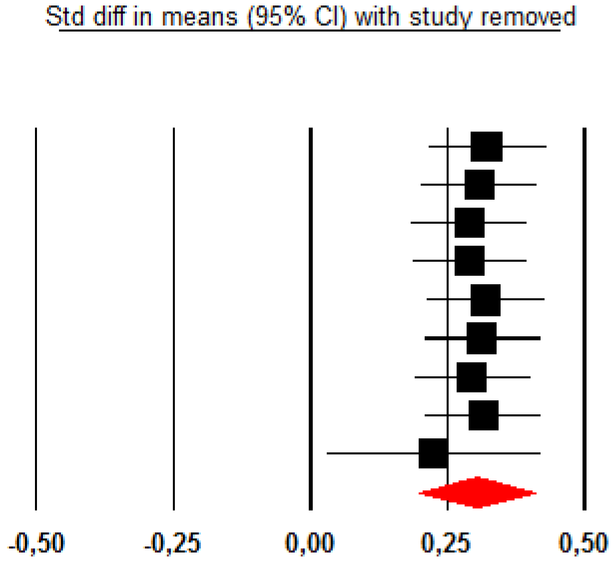

Figure 19: Sensitivity analyses for HL 2D:3D (Fixed-effect model)

7.3.3. Forest plots – 2D:5D

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
McFadden, 2003	0,646	0,221	0,049	0,213	1,079	2,922	0,003
McMechan, 2004	0,559	0,322	0,104	-0,073	1,191	1,734	0,083
Roney, 2004	0,489	0,380	0,145	-0,257	1,235	1,285	0,199
Manno, 2008	0,206	0,227	0,052	-0,239	0,651	0,907	0,365
Lombardo, 2008	0,060	0,283	0,080	-0,494	0,614	0,212	0,832
Auger, 2013	0,016	0,316	0,100	-0,603	0,636	0,052	0,959
	0,341	0,113	0,013	0,120	0,561	3,027	0,002

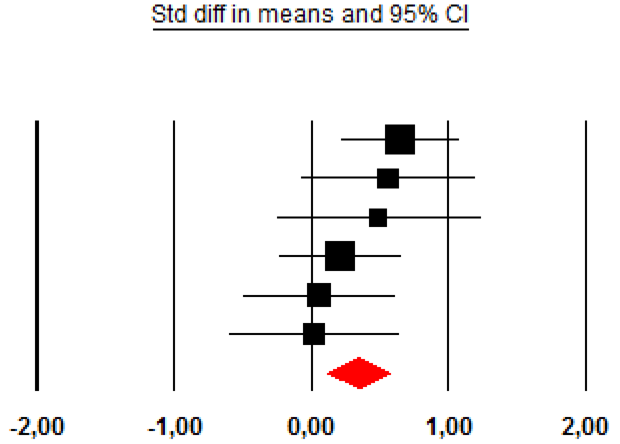

Figure 20: Forest plot for FR 2D:5D (Fixed-effect model)

Study name	Statistics with study removed							Std diff in means (95% CI) with study removed
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
McFadden, 2003	0,234	0,131	0,017	-0,023	0,490	1,788	0,074	
McMechan, 2004	0,310	0,120	0,014	0,075	0,546	2,584	0,010	
Roney, 2004	0,327	0,118	0,014	0,096	0,558	2,770	0,006	
Manno, 2008	0,385	0,130	0,017	0,131	0,639	2,968	0,003	
Lombardo, 2008	0,394	0,123	0,015	0,153	0,634	3,207	0,001	
Auger, 2013	0,388	0,120	0,015	0,152	0,624	3,219	0,001	
	0,341	0,113	0,013	0,120	0,561	3,027	0,002	

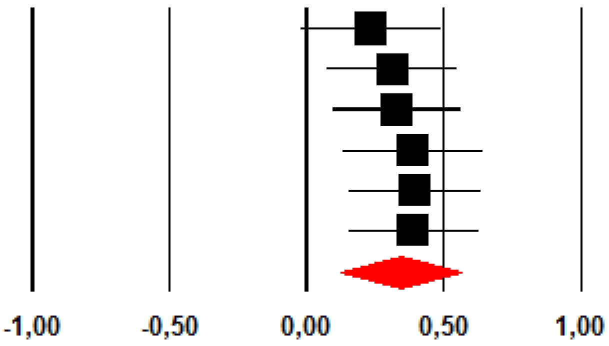

Figure 21: Sensitivity analysis for FR 2D:5D (Fixed-effect model)

Study name	Statistics for each study							Std diff in means and 95% CI
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
McFadden, 2003	0,614	0,221	0,049	0,182	1,046	2,784	0,005	
McMechan, 2003	0,197	0,317	0,100	-0,424	0,819	0,623	0,533	
Manno, 2008	0,361	0,228	0,052	-0,087	0,808	1,579	0,114	
Lombardo, 2008	0,090	0,283	0,080	-0,465	0,645	0,318	0,750	
Auger, 2013	0,302	0,318	0,101	-0,322	0,925	0,949	0,343	
	0,355	0,118	0,014	0,125	0,586	3,017	0,003	

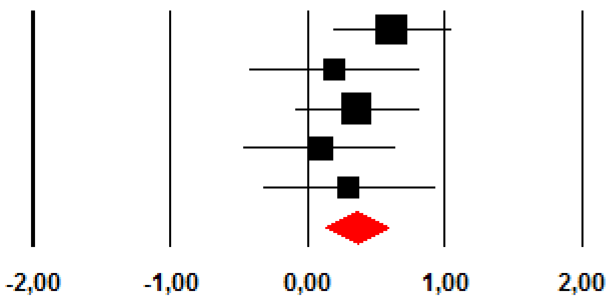

Figure 22: Forest plot for FL 2D:5D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,252	0,139	0,019	-0,021	0,525	1,810	0,070
McMechan, 2003	0,381	0,127	0,016	0,132	0,629	3,000	0,003
Manno, 2008	0,354	0,138	0,019	0,084	0,623	2,571	0,010
Lombardo, 2008	0,411	0,130	0,017	0,157	0,665	3,173	0,002
Auger, 2013	0,364	0,127	0,016	0,115	0,612	2,870	0,004
	0,355	0,118	0,014	0,125	0,586	3,017	0,003

Std diff in means (95% CI) with study removed

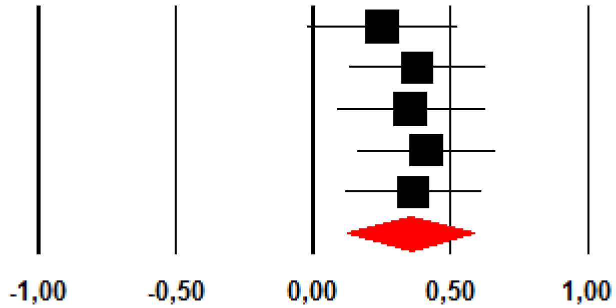

Figure 23: Sensitivity analysis for FL 2D:5D (Fixed-effect model)

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,021	0,197	0,039	-0,365	0,406	0,105	0,917
McFadden, 2003	0,601	0,216	0,047	0,178	1,024	2,783	0,005
Leoni, 2005	0,745	0,328	0,108	0,102	1,388	2,272	0,023
Manno, 2008	0,007	0,226	0,051	-0,436	0,451	0,033	0,974
Lombardo, 2008	0,710	0,292	0,085	0,138	1,282	2,435	0,015
	0,328	0,107	0,011	0,119	0,537	3,077	0,002

Std diff in means and 95% CI

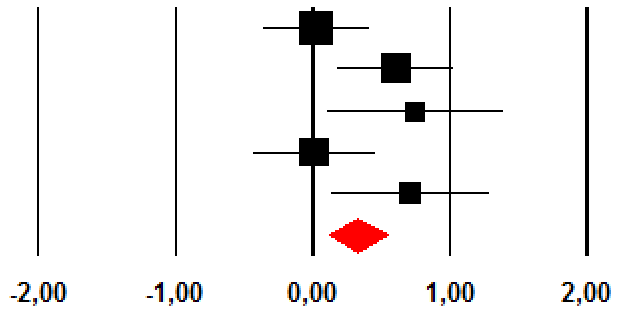

Figure 24: Forest plot for HR 2D:5D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,457	0,127	0,016	0,208	0,706	3,595	0,000
McFadden, 2003	0,240	0,123	0,015	-0,000	0,481	1,958	0,050
Leoni, 2005	0,279	0,113	0,013	0,058	0,500	2,472	0,013
Manno, 2008	0,420	0,121	0,015	0,183	0,657	3,471	0,001
Lombardo, 2008	0,269	0,115	0,013	0,045	0,494	2,349	0,019
	0,328	0,107	0,011	0,119	0,537	3,077	0,002

Std diff in means (95% CI) with study removed

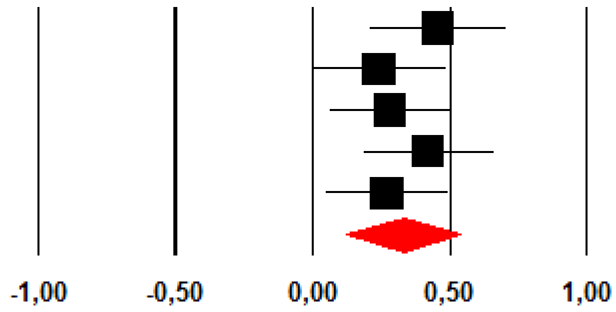

Figure 25: Sensitivity analysis for HR 2D:5D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,783	0,219	0,048	0,353	1,213	3,572	0,000
Manning, 2003	0,411	0,199	0,039	0,022	0,800	2,070	0,038
Leoni, 2005	0,237	0,319	0,102	-0,387	0,862	0,744	0,457
Manno, 2008	0,010	0,226	0,051	-0,433	0,454	0,046	0,963
Lombardo, 2008	0,000	0,283	0,080	-0,554	0,554	0,000	1,000
	0,332	0,107	0,011	0,124	0,541	3,119	0,002

Statistics for each study

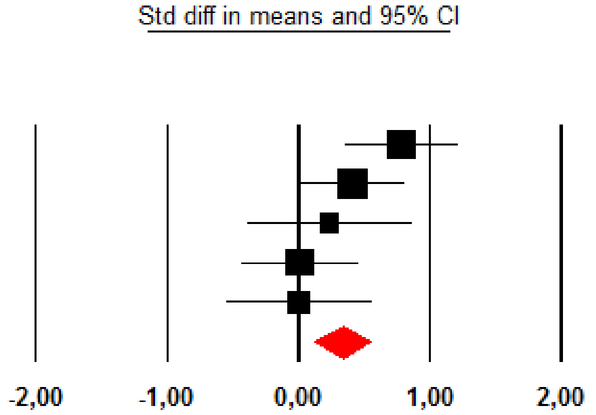

Figure 26: Forest plot for HL 2D:5D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,193	0,122	0,015	-0,046	0,432	1,581	0,114
Manning, 2003	0,301	0,126	0,016	0,053	0,548	2,379	0,017
Leoni, 2005	0,344	0,113	0,013	0,123	0,566	3,045	0,002
Manno, 2008	0,424	0,121	0,015	0,187	0,661	3,510	0,000
Lombardo, 2008	0,387	0,115	0,013	0,162	0,613	3,367	0,001
	0,332	0,107	0,011	0,124	0,541	3,119	0,002

Statistics with study removed

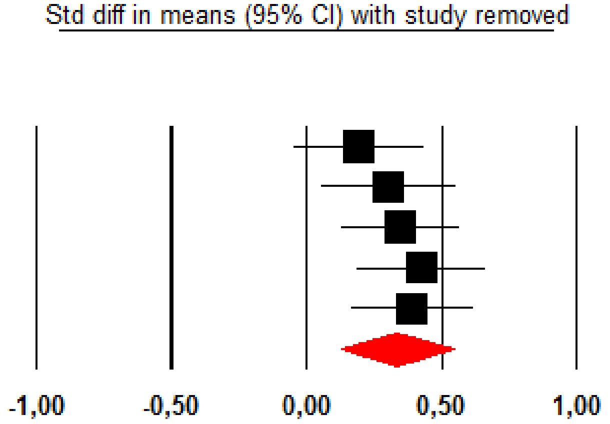

Figure 27: Sensitivity analysis for HL 2D:5D (Fixed-effect model)

7.3.4. Forest plots – 3D:4D

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,460	0,215	0,046	0,038	0,882	2,135	0,033
McMechan, 2003	0,149	0,317	0,100	-0,471	0,770	0,471	0,637
Roney, 2004	1,313	0,411	0,169	0,508	2,118	3,197	0,001
Rubolini, 2005 (1)	0,530	0,339	0,115	-0,135	1,195	1,563	0,118
Rubolini, 2005 (2)	0,210	0,388	0,151	-0,550	0,970	0,541	0,588
Manno, 2008	0,206	0,227	0,052	-0,239	0,651	0,907	0,365
Lombardo, 2008	0,020	0,283	0,080	-0,534	0,574	0,071	0,944
Auger, 2013	1,310	0,348	0,121	0,627	1,993	3,758	0,000
Balogova, 2015	0,141	0,250	0,063	-0,350	0,632	0,562	0,574
Van Damme, 2015	0,124	0,063	0,004	0,001	0,248	1,978	0,048
	0,367	0,120	0,014	0,131	0,602	3,053	0,002

Std diff in means and 95% CI

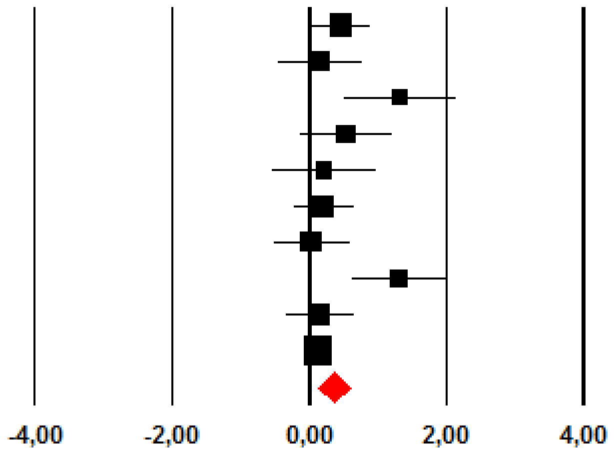

Figure 28: Forest plot for FR 3D:4D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
McFadden, 2003	0,361	0,134	0,018	0,098	0,623	2,693	0,007
McMechan, 2003	0,394	0,132	0,017	0,136	0,652	2,997	0,003
Roney, 2004	0,288	0,105	0,011	0,083	0,493	2,755	0,006
Rubolini, 2005 (1)	0,356	0,128	0,016	0,105	0,607	2,784	0,005
Rubolini, 2005 (2)	0,384	0,129	0,017	0,131	0,637	2,971	0,003
Manno, 2008	0,399	0,137	0,019	0,130	0,668	2,906	0,004
Lombardo, 2008	0,411	0,132	0,017	0,152	0,669	3,111	0,002
Auger, 2013	0,254	0,092	0,009	0,073	0,435	2,754	0,006
Balogova, 2015	0,404	0,135	0,018	0,139	0,669	2,985	0,003
Van Damme, 2015	0,430	0,142	0,020	0,152	0,707	3,036	0,002
	0,367	0,120	0,014	0,131	0,602	3,053	0,002

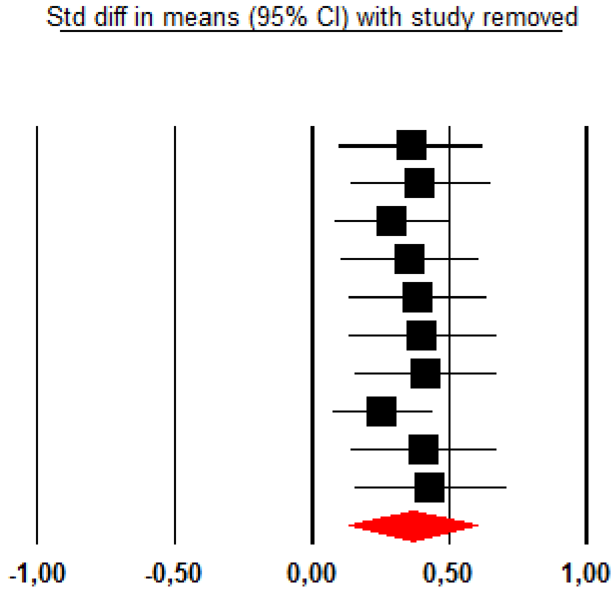

Figure 29: Sensitivity analysis for FR 3D:4D (Fixed-effect model)

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,492	0,216	0,047	0,069	0,915	2,280	0,023
McMechan, 2003	0,062	0,316	0,100	-0,558	0,682	0,196	0,845
Rubolini, 2005 (1)	0,210	0,334	0,112	-0,445	0,865	0,628	0,530
Rubolini, 2005 (2)	0,780	0,401	0,161	-0,005	1,565	1,946	0,052
Manno, 2008	0,361	0,228	0,052	-0,087	0,808	1,579	0,114
Lombardo, 2008	0,170	0,283	0,080	-0,385	0,725	0,600	0,549
Auger, 2013	0,896	0,332	0,110	0,245	1,546	2,700	0,007
Balogova, 2015	0,212	0,264	0,069	-0,305	0,728	0,804	0,422
Van Damme, 2015	0,006	0,063	0,004	-0,117	0,130	0,100	0,920
	0,112	0,053	0,003	0,008	0,216	2,109	0,035

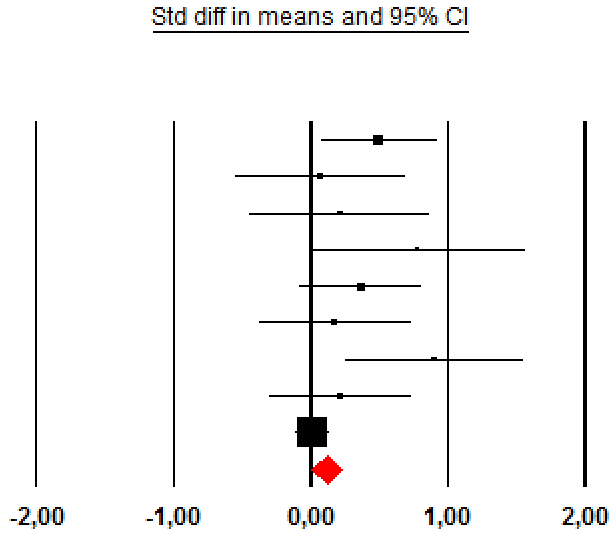

Figure 30: Forest plot for FL 3D:4D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,088	0,055	0,003	-0,020	0,195	1,598	0,110
McMechan, 2003	0,113	0,054	0,003	0,008	0,219	2,106	0,035
Rubolini, 2005 (1)	0,109	0,054	0,003	0,004	0,215	2,035	0,042
Rubolini, 2005 (2)	0,100	0,054	0,003	-0,005	0,205	1,868	0,062
Manno, 2008	0,098	0,055	0,003	-0,009	0,205	1,791	0,073
Lombardo, 2008	0,110	0,054	0,003	0,004	0,216	2,033	0,042
Auger, 2013	0,091	0,054	0,003	-0,014	0,197	1,699	0,089
Balogova, 2015	0,108	0,054	0,003	0,002	0,214	1,988	0,047
Van Damme, 2015	0,375	0,099	0,010	0,180	0,569	3,781	0,000
	0,112	0,053	0,003	0,008	0,216	2,109	0,035

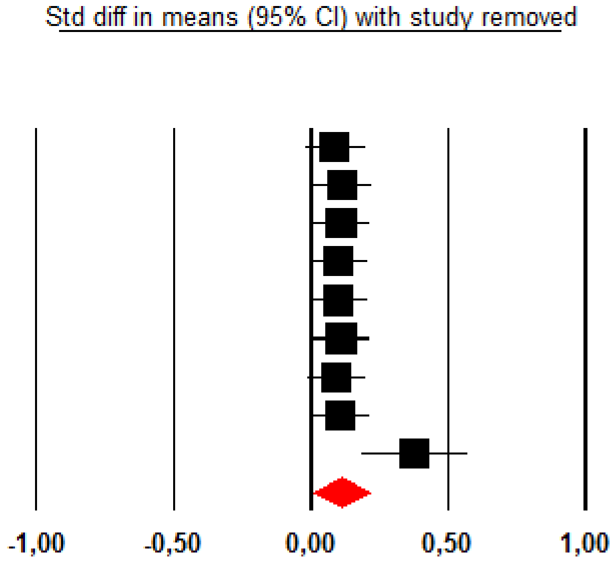

Figure 31: Sensitivity analysis FL 3D:4D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,235	0,197	0,039	-0,152	0,622	1,191	0,234
McFadden, 2003	0,354	0,216	0,047	-0,069	0,777	1,641	0,101
Leoni, 2005	0,162	0,318	0,101	-0,461	0,786	0,511	0,610
Saino, 2007	0,906	0,312	0,097	0,295	1,518	2,903	0,004
Manno, 2008	0,007	0,226	0,051	-0,436	0,451	0,033	0,974
Lombardo, 2008	0,320	0,285	0,081	-0,238	0,878	1,124	0,261
Leoni, 2008	0,202	0,249	0,062	-0,287	0,691	0,810	0,418
Bogdan, 2009	0,235	0,183	0,033	-0,124	0,594	1,284	0,199
Ruuskanen, 2011	0,000	0,105	0,011	-0,206	0,206	0,000	1,000
Tobler, 2011	0,442	0,177	0,031	0,096	0,788	2,504	0,012
Balogova, 2015	0,017	0,257	0,066	-0,487	0,521	0,066	0,947
Van Damme, 2015	0,264	0,063	0,004	0,141	0,388	4,189	0,000
	0,224	0,043	0,002	0,140	0,309	5,182	0,000

Statistics for each study

Std diff in means and 95% CI

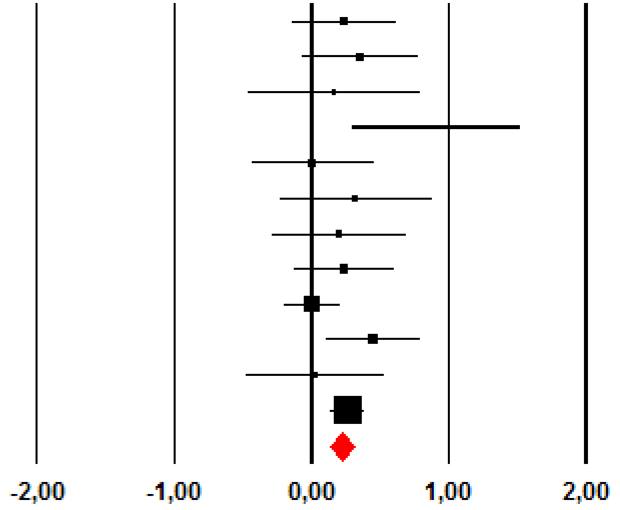

Figure 32: Forest plot for HR 3D:4D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,224	0,044	0,002	0,137	0,311	5,044	0,000
McFadden, 2003	0,219	0,044	0,002	0,132	0,306	4,954	0,000
Leoni, 2005	0,226	0,044	0,002	0,140	0,311	5,161	0,000
Saino, 2007	0,211	0,044	0,002	0,125	0,297	4,826	0,000
Manno, 2008	0,233	0,044	0,002	0,146	0,319	5,273	0,000
Lombardo, 2008	0,222	0,044	0,002	0,136	0,308	5,070	0,000
Leoni, 2008	0,225	0,044	0,002	0,139	0,311	5,119	0,000
Bogdan, 2009	0,224	0,045	0,002	0,136	0,311	5,021	0,000
Ruuskanen, 2011	0,270	0,048	0,002	0,177	0,363	5,686	0,000
Tobler, 2011	0,210	0,045	0,002	0,123	0,298	4,712	0,000
Balogova, 2015	0,230	0,044	0,002	0,144	0,317	5,246	0,000
Van Damme, 2015	0,189	0,059	0,004	0,072	0,305	3,173	0,002
	0,224	0,043	0,002	0,140	0,309	5,182	0,000

Std diff in means (95% CI) with study removed

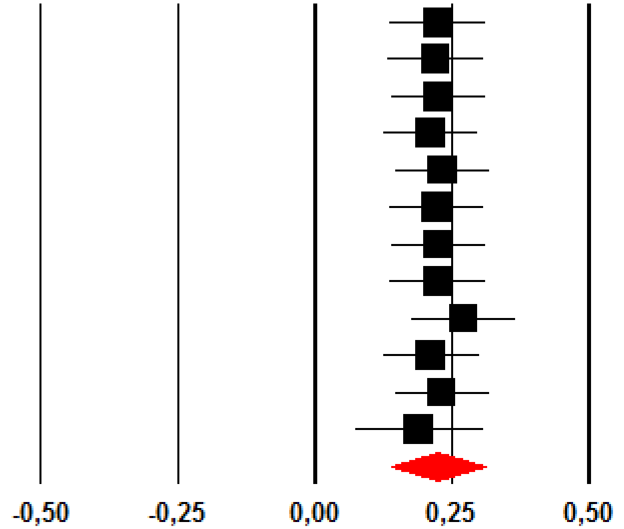

Figure 33: Sensitivity analysis HR 3D:4D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,437	0,217	0,047	0,012	0,862	2,017	0,044
Manning, 2003	0,250	0,197	0,039	-0,137	0,637	1,267	0,205
Leoni, 2005	0,159	0,318	0,101	-0,464	0,783	0,500	0,617
Saino, 2007	0,474	0,302	0,091	-0,118	1,066	1,569	0,117
Manno, 2008	0,010	0,226	0,051	-0,433	0,454	0,046	0,963
Lombardo, 2008	0,510	0,287	0,083	-0,053	1,073	1,775	0,076
Leoni, 2008	0,202	0,249	0,062	-0,287	0,691	0,810	0,418
Tobler, 2011	0,387	0,176	0,031	0,043	0,731	2,202	0,028
Balogova, 2015	0,060	0,258	0,067	-0,446	0,567	0,233	0,816
Van Damme, 2015	0,338	0,063	0,004	0,214	0,462	5,338	0,000
	0,315	0,049	0,002	0,218	0,411	6,396	0,000

Statistics for each study

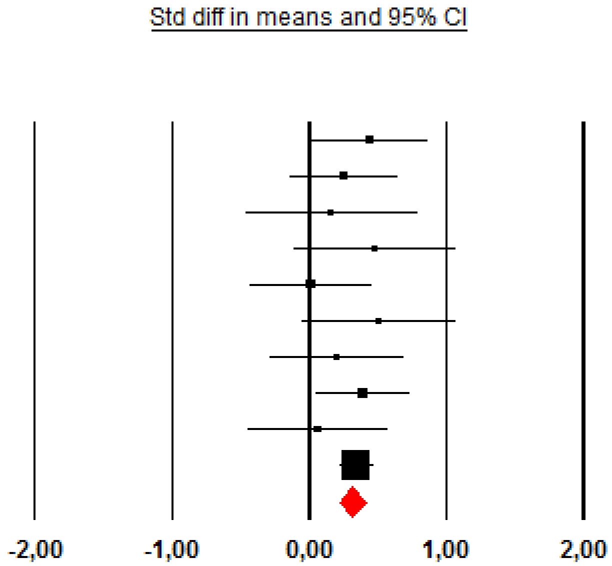

Figure 34: Forest plot for HL 3D:4D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
McFadden, 2003	0,308	0,051	0,003	0,209	0,407	6,097	0,000
Manning, 2003	0,319	0,051	0,003	0,220	0,419	6,279	0,000
Leoni, 2005	0,319	0,050	0,002	0,221	0,416	6,396	0,000
Saino, 2007	0,311	0,050	0,002	0,213	0,408	6,223	0,000
Manno, 2008	0,330	0,050	0,003	0,231	0,429	6,543	0,000
Lombardo, 2008	0,309	0,050	0,002	0,211	0,407	6,183	0,000
Leoni, 2008	0,320	0,050	0,003	0,221	0,418	6,361	0,000
Tobler, 2011	0,309	0,051	0,003	0,208	0,409	6,020	0,000
Balogova, 2015	0,325	0,050	0,003	0,226	0,423	6,470	0,000
Van Damme, 2015	0,280	0,078	0,006	0,126	0,433	3,570	0,000
	0,315	0,049	0,002	0,218	0,411	6,396	0,000

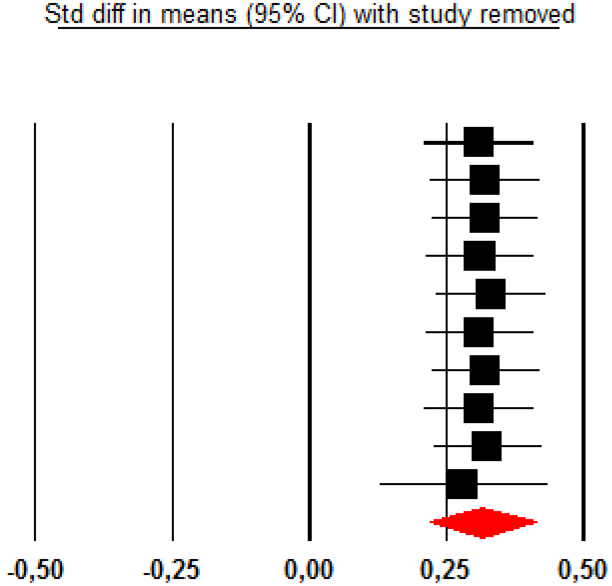

Figure 35: Sensitivity analysis HL 3D:4D (Fixed-effect model)

7.3.5. Forest plots – 3D:5D

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,937	0,226	0,051	0,494	1,380	4,148	0,000
McMechan, 2004	0,360	0,319	0,102	-0,265	0,985	1,129	0,259
Roney, 2004	0,340	0,378	0,143	-0,401	1,081	0,900	0,368
Manno, 2008	0,239	0,227	0,052	-0,206	0,685	1,053	0,292
Lombardo, 2008	0,283	0,284	0,081	-0,274	0,840	0,995	0,320
Auger, 2013	0,368	0,319	0,102	-0,257	0,993	1,153	0,249
	0,462	0,113	0,013	0,240	0,684	4,080	0,000

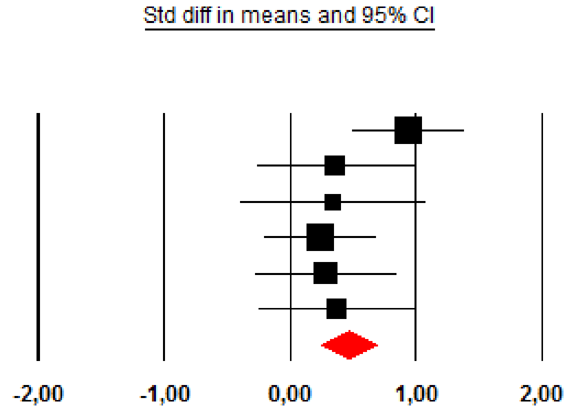

Figure 36: Forest plot for FR 3D:5D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,303	0,131	0,017	0,046	0,559	2,312	0,021
McMechan, 2004	0,477	0,121	0,015	0,239	0,714	3,935	0,000
Roney, 2004	0,474	0,119	0,014	0,241	0,707	3,993	0,000
Manno, 2008	0,535	0,131	0,017	0,279	0,791	4,100	0,000
Lombardo, 2008	0,496	0,123	0,015	0,254	0,738	4,016	0,000
Auger, 2013	0,475	0,121	0,015	0,238	0,713	3,926	0,000
	0,462	0,113	0,013	0,240	0,684	4,080	0,000

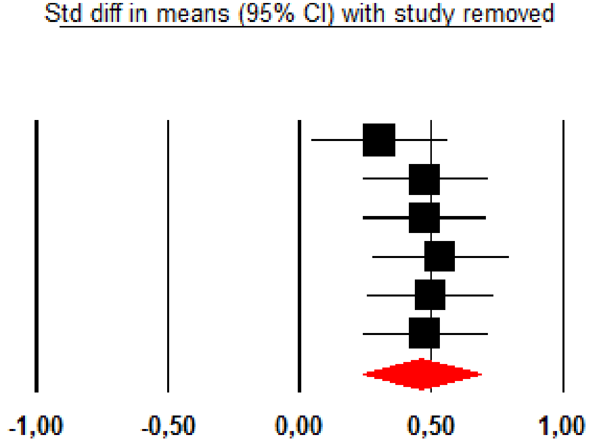

Figure 37: Sensitivity analysis for FR 3D:5D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
McFadden, 2003	0,749	0,222	0,049	0,314	1,184	3,375	0,001
McMechan, 2004	0,413	0,320	0,102	-0,214	1,039	1,291	0,197
Manno, 2008	0,509	0,230	0,053	0,058	0,960	2,212	0,027
Lombardo, 2008	0,048	0,283	0,080	-0,506	0,603	0,170	0,865
Auger, 2013	0,050	0,316	0,100	-0,570	0,670	0,158	0,874
	0,419	0,118	0,014	0,187	0,651	3,545	0,000

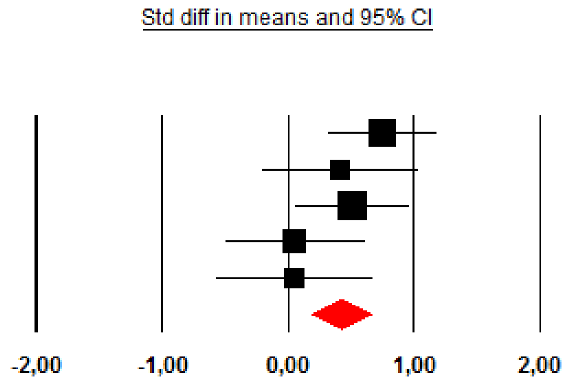

Figure 38: Forest plot for FL 3D:5D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
McFadden, 2003	0,288	0,140	0,020	0,014	0,562	2,063	0,039
McMechan, 2004	0,420	0,127	0,016	0,171	0,670	3,301	0,001
Manno, 2008	0,387	0,138	0,019	0,117	0,657	2,806	0,005
Lombardo, 2008	0,498	0,130	0,017	0,243	0,753	3,824	0,000
Auger, 2013	0,479	0,128	0,016	0,229	0,729	3,758	0,000
	0,419	0,118	0,014	0,187	0,651	3,545	0,000

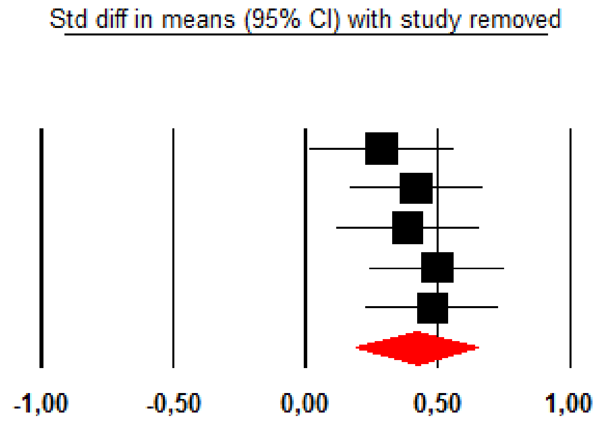

Figure 39: Sensitivity Analysis – FL 3D:5D (Fixed-effect model)

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,061	0,197	0,039	-0,325	0,446	0,310	0,757
McFadden, 2003	0,390	0,216	0,047	-0,034	0,814	1,805	0,071
Leoni, 2005	0,257	0,319	0,102	-0,368	0,883	0,807	0,420
Lombardo, 2008	0,648	0,290	0,084	0,079	1,216	2,232	0,026
Manno, 2008	0,029	0,226	0,051	-0,414	0,473	0,130	0,897
	0,234	0,106	0,011	0,026	0,443	2,203	0,028

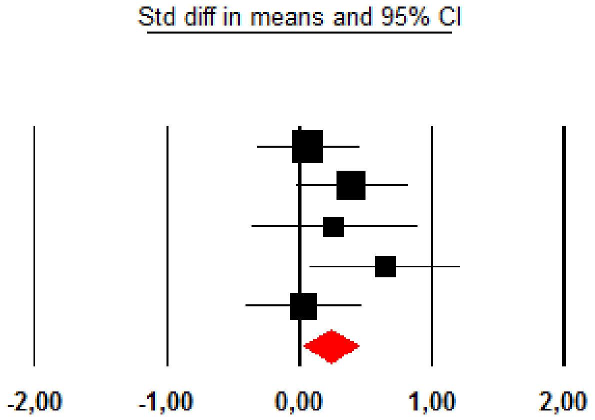

Figure 40: Forest plot for HR 3D:5D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,306	0,126	0,016	0,058	0,553	2,420	0,016
McFadden, 2003	0,185	0,122	0,015	-0,055	0,424	1,511	0,131
Leoni, 2005	0,231	0,113	0,013	0,010	0,452	2,052	0,040
Lombardo, 2008	0,170	0,114	0,013	-0,054	0,394	1,489	0,136
Manno, 2008	0,292	0,120	0,015	0,056	0,528	2,426	0,015
	0,234	0,106	0,011	0,026	0,443	2,203	0,028

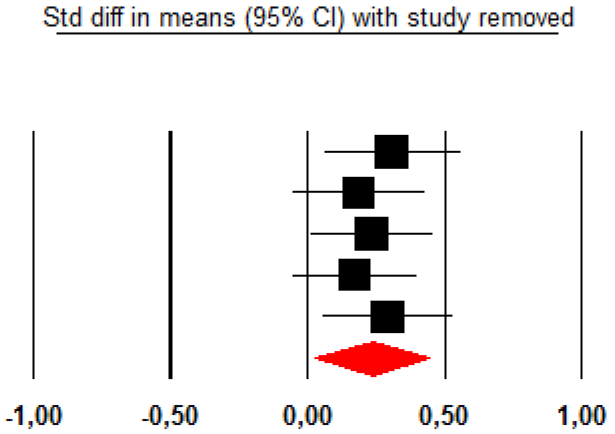

Figure 41: Sensitivity analysis – HR 3D:5D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,045	0,197	0,039	-0,340	0,431	0,230	0,818
McFadden, 2003	0,531	0,218	0,047	0,104	0,958	2,438	0,015
Leoni, 2005	0,254	0,319	0,102	-0,371	0,879	0,797	0,425
Manno, 2008	0,104	0,227	0,051	-0,340	0,548	0,460	0,646
Lombardo, 2008	0,215	0,284	0,080	-0,341	0,771	0,758	0,449
	0,221	0,106	0,011	0,012	0,429	2,078	0,038

Statistics for each study

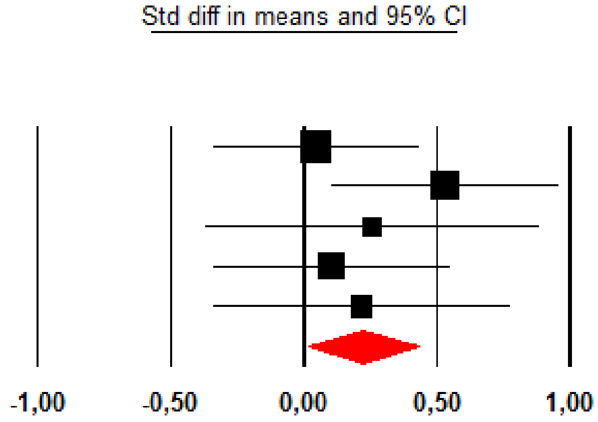

Figure 42: Forest plot for HL 3D:5D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,293	0,126	0,016	0,046	0,540	2,321	0,020
McFadden, 2003	0,124	0,122	0,015	-0,115	0,362	1,018	0,309
Leoni, 2005	0,216	0,113	0,013	-0,004	0,437	1,922	0,055
Manno, 2008	0,253	0,120	0,014	0,018	0,489	2,108	0,035
Lombardo, 2008	0,222	0,115	0,013	-0,003	0,446	1,935	0,053
	0,221	0,106	0,011	0,012	0,429	2,078	0,038

Statistics with study removed

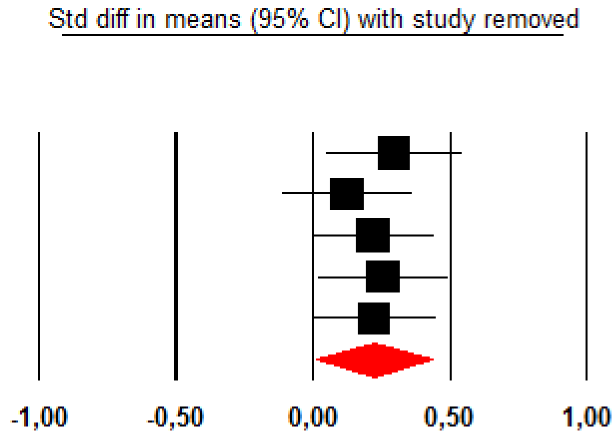

Figure 43: Sensitivity analysis – HL 3D:5D (Fixed-effect model)

7.3.6. Forest plots – 4D:5D

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
McFadden, 2003	0,933	0,227	0,051	0,488	1,378	4,112	0,000
McMechan, 2003	0,764	0,328	0,107	0,122	1,406	2,331	0,020
Roney, 2004	1,120	0,401	0,161	0,333	1,907	2,790	0,005
Manno, 2008	0,421	0,229	0,052	-0,028	0,870	1,840	0,066
Lombardo, 2008	0,170	0,283	0,080	-0,386	0,725	0,599	0,549
Auger, 2013	1,097	0,339	0,115	0,432	1,762	3,234	0,001
	0,690	0,115	0,013	0,464	0,916	5,983	0,000

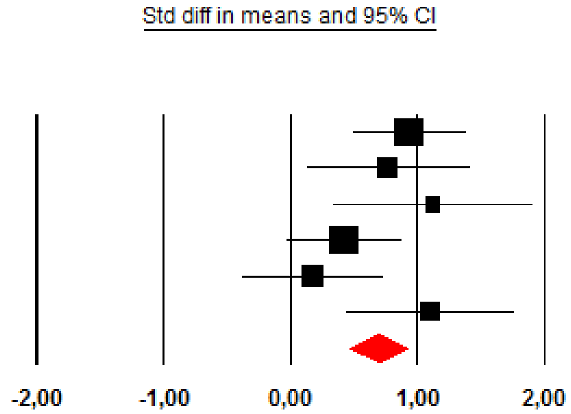

Figure 44: Forest plot for FR 4D:5D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,605	0,134	0,018	0,343	0,868	4,520	0,000
McMechan, 2003	0,680	0,123	0,015	0,438	0,921	5,515	0,000
Roney, 2004	0,651	0,120	0,014	0,415	0,887	5,409	0,000
Manno, 2008	0,781	0,134	0,018	0,520	1,043	5,853	0,000
Lombardo, 2008	0,793	0,126	0,016	0,546	1,041	6,283	0,000
Auger, 2013	0,637	0,123	0,015	0,396	0,877	5,193	0,000
	0,690	0,115	0,013	0,464	0,916	5,983	0,000

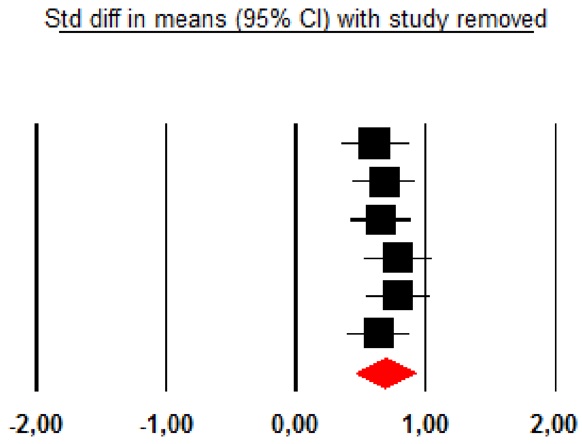

Figure 45: Sensitivity analysis for FR 4D:5D (Fixed-effect model)

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,619	0,221	0,049	0,187	1,051	2,806	0,005
McMechan, 2004	0,518	0,321	0,103	-0,112	1,148	1,612	0,107
Manno, 2008	0,257	0,227	0,052	-0,189	0,702	1,129	0,259
Lombardo, 2008	0,034	0,283	0,080	-0,520	0,588	0,120	0,904
Auger, 2013	0,284	0,318	0,101	-0,338	0,907	0,895	0,371
	0,360	0,118	0,014	0,129	0,591	3,058	0,002

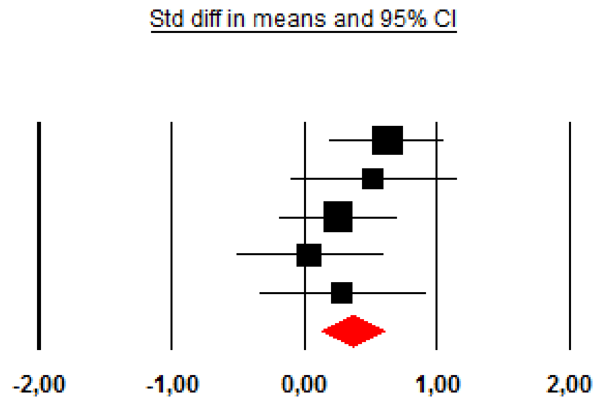

Figure 46: Forest plot for FL 4D:5D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
McFadden, 2003	0,257	0,139	0,019	-0,016	0,530	1,844	0,065
McMechan, 2004	0,336	0,127	0,016	0,088	0,584	2,651	0,008
Manno, 2008	0,399	0,138	0,019	0,128	0,669	2,891	0,004
Lombardo, 2008	0,429	0,130	0,017	0,175	0,683	3,309	0,001
Auger, 2013	0,373	0,127	0,016	0,124	0,621	2,935	0,003
	0,360	0,118	0,014	0,129	0,591	3,058	0,002

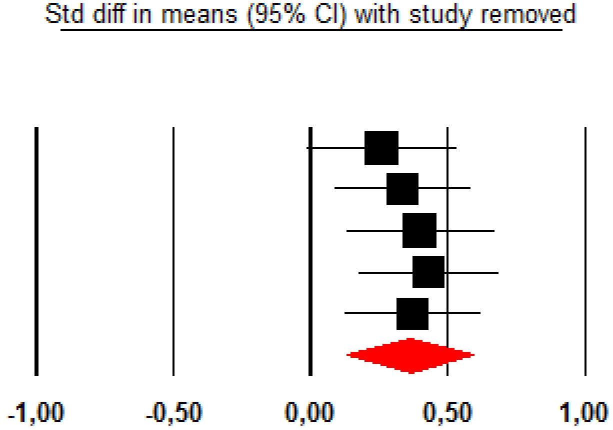

Figure 47: Sensitivity analysis for FL 4D:5D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
Manning, 2003	0,189	0,197	0,039	-0,197	0,575	0,958	0,338
McFadden, 2003	0,760	0,220	0,048	0,329	1,191	3,457	0,001
Leoni, 2005	0,273	0,319	0,102	-0,352	0,899	0,856	0,392
Manno, 2008	0,069	0,227	0,051	-0,375	0,513	0,303	0,762
Lombardo, 2008	0,659	0,290	0,084	0,090	1,228	2,269	0,023
	0,370	0,107	0,011	0,161	0,579	3,464	0,001

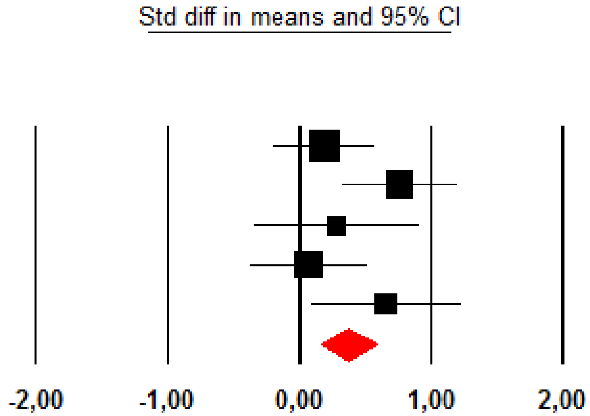

Figure 48: Forest plot for HR 4D:5D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,446	0,127	0,016	0,196	0,695	3,504	0,000
McFadden, 2003	0,250	0,122	0,015	0,010	0,489	2,041	0,041
Leoni, 2005	0,382	0,113	0,013	0,160	0,605	3,372	0,001
Manno, 2008	0,456	0,121	0,015	0,219	0,694	3,766	0,000
Lombardo, 2008	0,325	0,115	0,013	0,100	0,550	2,827	0,005
	0,370	0,107	0,011	0,161	0,579	3,464	0,001

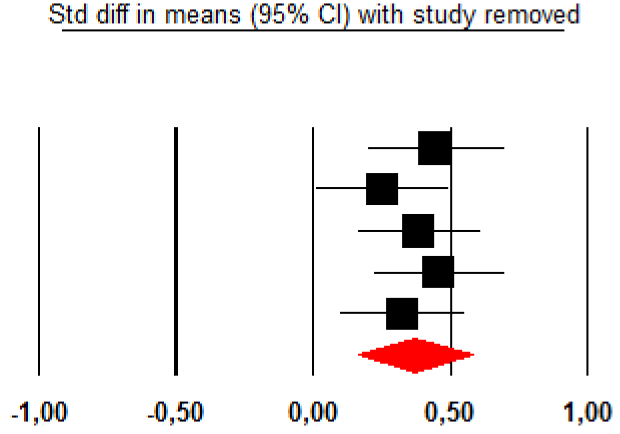

Figure 49: Sensitivity analysis for HR 4D:5D (Fixed-effect model)

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,130	0,197	0,039	-0,256	0,516	0,659	0,510
McFadden, 2003	0,844	0,222	0,049	0,410	1,278	3,809	0,000
Leoni, 2005	0,006	0,318	0,101	-0,616	0,629	0,020	0,984
Manno, 2008	0,132	0,227	0,051	-0,313	0,576	0,580	0,562
Lombardo, 2008	0,585	0,289	0,083	0,019	1,152	2,027	0,043
	0,345	0,107	0,011	0,135	0,554	3,226	0,001

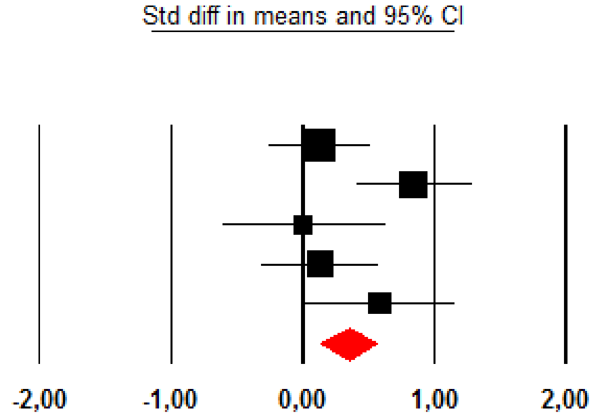

Figure 50: Forest plot for HL 4D:5D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manning, 2003	0,435	0,127	0,016	0,185	0,684	3,416	0,001
McFadden, 2003	0,193	0,122	0,015	-0,046	0,433	1,585	0,113
Leoni, 2005	0,388	0,114	0,013	0,166	0,611	3,419	0,001
Manno, 2008	0,406	0,121	0,015	0,168	0,643	3,348	0,001
Lombardo, 2008	0,307	0,115	0,013	0,081	0,532	2,665	0,008
	0,345	0,107	0,011	0,135	0,554	3,226	0,001

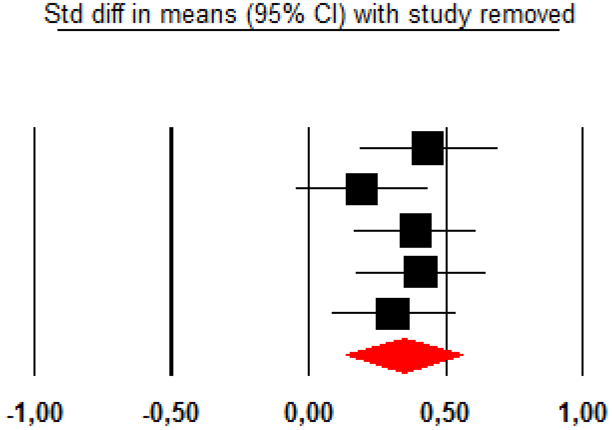

Figure 51: Sensitivity analysis for HL 4D:5D (Fixed-effect model)

7.3.7. *Forest plots – 1D:2D*

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,276	0,220	0,049	-0,156	0,708	1,253	0,210
Manno, 2008	0,542	0,231	0,053	0,090	0,994	2,349	0,019
Lombardo, 2008	0,256	0,284	0,081	-0,300	0,813	0,902	0,367
	0,368	0,139	0,019	0,095	0,640	2,647	0,008

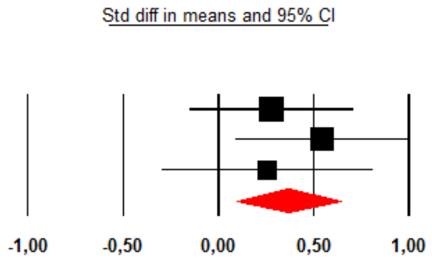

Figure 52: Forest plot for FR 1D:2D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,428	0,179	0,032	0,077	0,779	2,392	0,017
Manno, 2008	0,269	0,174	0,030	-0,073	0,610	1,543	0,123
Lombardo, 2008	0,403	0,159	0,025	0,091	0,715	2,529	0,011
	0,368	0,139	0,019	0,095	0,640	2,647	0,008

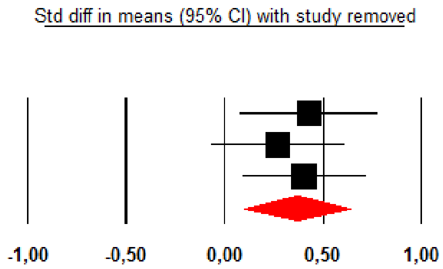

Figure 53: Sensitivity analysis – FR 1D:2D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,516	0,223	0,050	0,079	0,953	2,316	0,021
Manno, 2008	0,226	0,227	0,052	-0,219	0,671	0,995	0,320
Lombardo, 2008	0,372	0,285	0,081	-0,187	0,931	1,305	0,192
	0,373	0,139	0,019	0,101	0,646	2,688	0,007

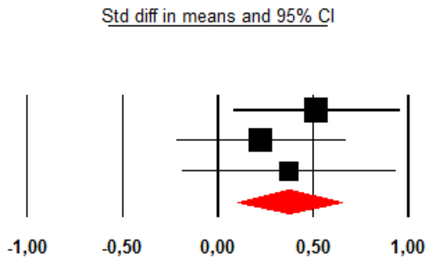

Figure 54: Forest plot for FL 1D:2D (Fixed-effect model)

Study name	Statistics with study removed							Std diff in means (95% CI) with study removed
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
McFadden, 2003	0,283	0,178	0,032	-0,066	0,631	1,591	0,112	
Manno, 2008	0,462	0,176	0,031	0,117	0,806	2,629	0,009	
Lombardo, 2008	0,374	0,159	0,025	0,062	0,686	2,350	0,019	
	0,373	0,139	0,019	0,101	0,646	2,688	0,007	

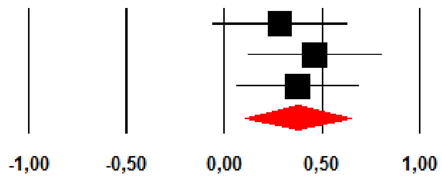

Figure 55: Sensitivity analysis – FL 1D:2D (Fixed-effect model)

Study name	Statistics for each study							Std diff in means and 95% CI
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
McFadden, 2003	0,110	0,222	0,049	-0,325	0,545	0,495	0,620	
Manno, 2008	0,245	0,227	0,052	-0,200	0,691	1,078	0,281	
Lombardo, 2008	0,326	0,285	0,081	-0,232	0,884	1,144	0,253	
	0,211	0,139	0,019	-0,060	0,483	1,525	0,127	

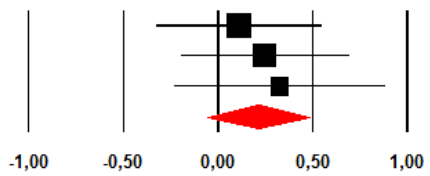

Figure 56: Forest plot for HR 1D:2D (Fixed-effect model)

Study name	Statistics with study removed							Std diff in means (95% CI) with study removed
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
McFadden, 2003	0,276	0,178	0,032	-0,072	0,625	1,556	0,120	
Manno, 2008	0,192	0,175	0,031	-0,152	0,535	1,094	0,274	
Lombardo, 2008	0,176	0,159	0,025	-0,135	0,487	1,108	0,268	
	0,211	0,139	0,019	-0,060	0,483	1,525	0,127	

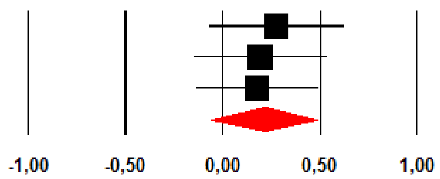

Figure 57: Sensitivity analysis – HR 1D:2D (Fixed-effect model)

7.3.8. Forest plots – 1D:3D

Study name	Statistics for each study							Std diff in means and 95% CI
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
McFadden, 2003	0,337	0,220	0,048	-0,094	0,768	1,534	0,125	
Manno, 2008	0,505	0,230	0,053	0,054	0,955	2,193	0,028	
Lombardo, 2008	0,596	0,289	0,084	0,030	1,163	2,062	0,039	
	0,459	0,139	0,019	0,186	0,731	3,293	0,001	

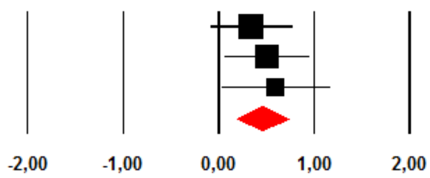

Figure 58: Forest plot for FR 1D:3D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
McFadden, 2003	0,540	0,180	0,032	0,187	0,893	3,000	0,003
Manno, 2008	0,432	0,175	0,031	0,089	0,775	2,469	0,014
Lombardo, 2008	0,417	0,159	0,025	0,106	0,728	2,624	0,009
	0,459	0,139	0,019	0,186	0,731	3,293	0,001

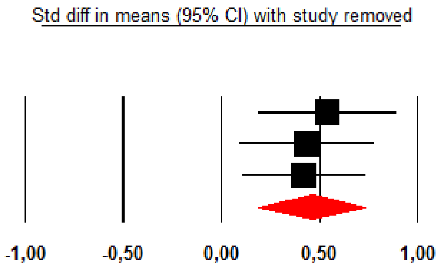

Figure 59: Sensitivity analysis – FR 1D:3D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
McFadden, 2003	0,400	0,220	0,049	-0,032	0,832	1,816	0,069
Manno, 2008	0,161	0,227	0,051	-0,283	0,606	0,712	0,477
Lombardo, 2008	0,389	0,286	0,082	-0,170	0,949	1,363	0,173
	0,309	0,138	0,019	0,038	0,580	2,234	0,026

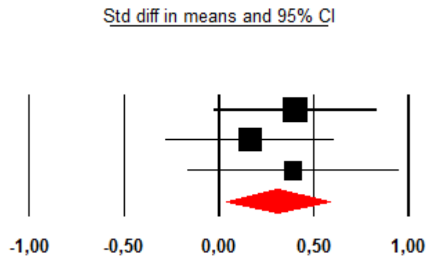

Figure 60: Forest plot for FL 1D:3D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
McFadden, 2003	0,250	0,178	0,032	-0,098	0,598	1,405	0,160
Manno, 2008	0,396	0,174	0,030	0,054	0,738	2,270	0,023
Lombardo, 2008	0,284	0,158	0,025	-0,026	0,594	1,798	0,072
	0,309	0,138	0,019	0,038	0,580	2,234	0,026

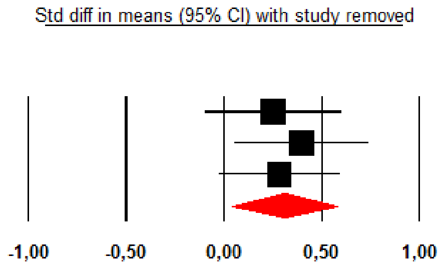

Figure 61: Sensitivity analysis – FL 1D:3D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
McFadden, 2003	0,106	0,226	0,051	-0,336	0,548	0,470	0,638
Manno, 2008	0,223	0,227	0,052	-0,223	0,668	0,980	0,327
Lombardo, 2008	0,188	0,283	0,080	-0,367	0,744	0,664	0,506
Genovart, 2008	0,026	0,140	0,020	-0,248	0,300	0,189	0,850
	0,098	0,099	0,010	-0,095	0,292	0,996	0,319

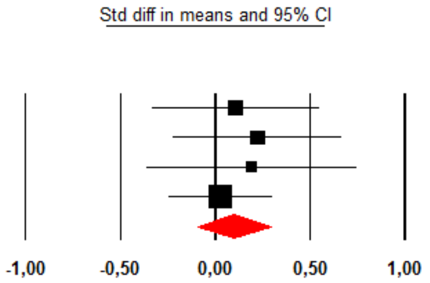

Figure 62: Forest plot for HR 1D:3D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
McFadden, 2003	0,096	0,110	0,012	-0,119	0,312	0,879	0,379
Manno, 2008	0,069	0,110	0,012	-0,145	0,284	0,633	0,527
Lombardo, 2008	0,086	0,105	0,011	-0,120	0,292	0,816	0,415
Genovart, 2008	0,170	0,139	0,019	-0,103	0,443	1,218	0,223
	0,098	0,099	0,010	-0,095	0,292	0,996	0,319

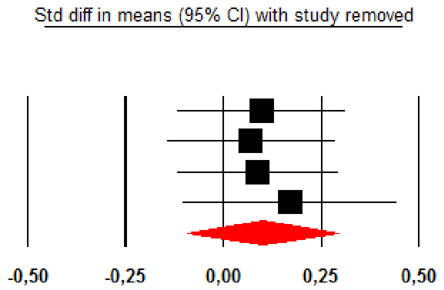

Figure 63: Sensitivity analysis – HR 1D:3D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
McFadden, 2003	0,212	0,226	0,051	-0,231	0,655	0,938	0,348
Manno, 2008	0,274	0,228	0,052	-0,172	0,720	1,205	0,228
Lombardo, 2008	0,057	0,283	0,080	-0,497	0,612	0,203	0,839
Genovart, 2008	0,026	0,140	0,020	-0,248	0,300	0,189	0,850
	0,112	0,099	0,010	-0,081	0,306	1,137	0,255

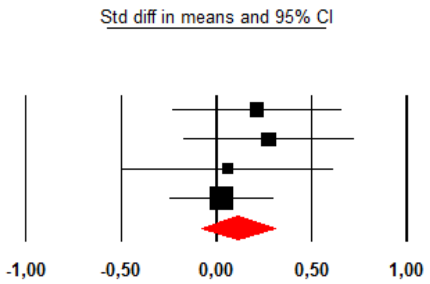

Figure 64: Forest plot for HL 1D:3D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics with study removed						
McFadden, 2003	0,089	0,110	0,012	-0,126	0,304	0,809	0,419
Manno, 2008	0,075	0,110	0,012	-0,140	0,290	0,682	0,495
Lombardo, 2008	0,120	0,105	0,011	-0,087	0,326	1,138	0,255
Genovart, 2008	0,198	0,139	0,019	-0,076	0,471	1,418	0,156
	0,112	0,099	0,010	-0,081	0,306	1,137	0,255

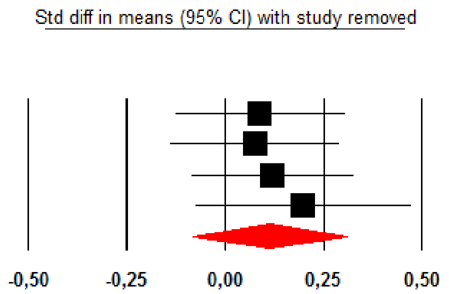

Figure 65: Sensitivity analysis – HL 1D:3D (Fixed-effect model)

7.3.9. *Forest plots – 1D:4D*

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,166	0,220	0,048	-0,264	0,596	0,756	0,450
Manno, 2008	0,539	0,231	0,053	0,087	0,991	2,339	0,019
Lombardo, 2008	0,414	0,286	0,082	-0,147	0,974	1,447	0,148
	0,360	0,139	0,019	0,088	0,632	2,592	0,010

Statistics for each study

Std diff in means and 95% CI

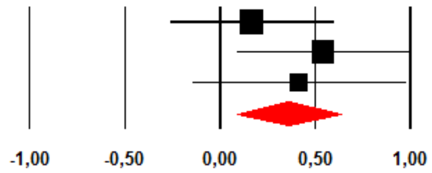

Figure 66: Forest plot for FR 1D:4D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,490	0,179	0,032	0,138	0,841	2,729	0,006
Manno, 2008	0,258	0,174	0,030	-0,083	0,599	1,481	0,139
Lombardo, 2008	0,344	0,159	0,025	0,032	0,655	2,161	0,031
	0,360	0,139	0,019	0,088	0,632	2,592	0,010

Statistics with study removed

Std diff in means (95% CI) with study removed

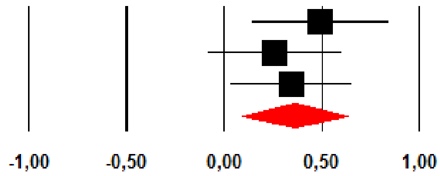

Figure 67: Sensitivity analysis – FR 1D:4D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,226	0,220	0,048	-0,205	0,657	1,028	0,304
Manno, 2008	0,029	0,226	0,051	-0,415	0,473	0,128	0,898
Lombardo, 2008	0,431	0,286	0,082	-0,130	0,992	1,507	0,132
	0,201	0,138	0,019	-0,070	0,471	1,451	0,147

Statistics for each study

Std diff in means and 95% CI

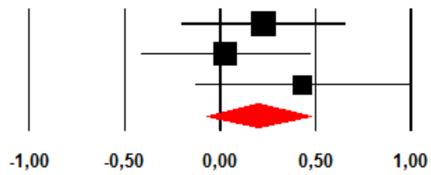

Figure 68: Forest plot for FL 1D:4D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,184	0,178	0,032	-0,164	0,532	1,036	0,300
Manno, 2008	0,302	0,174	0,030	-0,040	0,644	1,733	0,083
Lombardo, 2008	0,130	0,158	0,025	-0,179	0,440	0,826	0,409
	0,201	0,138	0,019	-0,070	0,471	1,451	0,147

Std diff in means (95% CI) with study removed

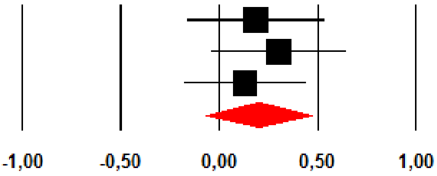

Figure 69: Sensitivity analysis – FL 1D:4D (Fixed-effect model)

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,066	0,223	0,050	-0,371	0,503	0,296	0,767
Manno, 2008	0,144	0,227	0,051	-0,301	0,588	0,633	0,527
Lombardo, 2008	0,096	0,283	0,080	-0,459	0,650	0,338	0,735
	0,102	0,139	0,019	-0,170	0,374	0,737	0,461

Std diff in means and 95% CI

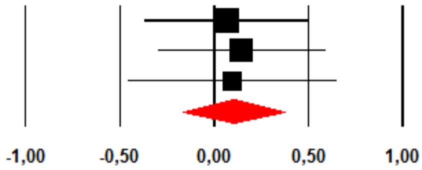

Figure 70: Forest plot for HR 1D:4D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,125	0,177	0,031	-0,222	0,472	0,706	0,480
Manno, 2008	0,077	0,175	0,031	-0,266	0,421	0,442	0,659
Lombardo, 2008	0,104	0,159	0,025	-0,208	0,416	0,655	0,512
	0,102	0,139	0,019	-0,170	0,374	0,737	0,461

Std diff in means (95% CI) with study removed

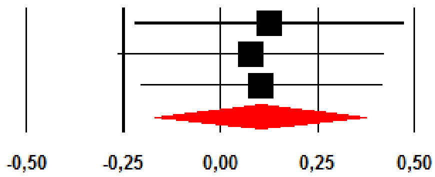

Figure 71: Sensitivity analysis – HR 1D:4D (Fixed-effect model)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,017	0,223	0,050	-0,420	0,454	0,076	0,939
Manno, 2008	0,260	0,227	0,052	-0,185	0,706	1,145	0,252
Lombardo, 2008	0,217	0,284	0,080	-0,339	0,773	0,765	0,444
	0,156	0,139	0,019	-0,116	0,428	1,121	0,262

Statistics for each study

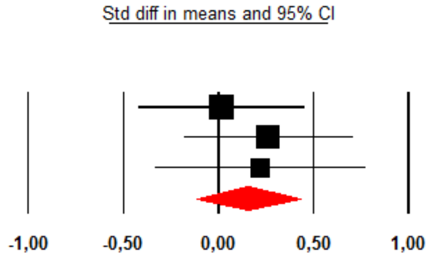

Figure 72: Forest plot for HL 1D:4D (Fixed-effect model)

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,243	0,177	0,031	-0,104	0,591	1,372	0,170
Manno, 2008	0,093	0,175	0,031	-0,250	0,437	0,533	0,594
Lombardo, 2008	0,136	0,159	0,025	-0,176	0,448	0,856	0,392
	0,156	0,139	0,019	-0,116	0,428	1,121	0,262

Statistics with study removed

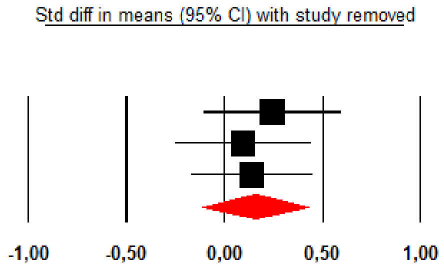

Figure 73: Sensitivity analysis – HL 1D:4D (Fixed-effect model)

7.3.10. Forest plots – 1D:5D

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,267	0,222	0,049	-0,169	0,703	1,200	0,230
Manno, 2008	0,337	0,228	0,052	-0,110	0,783	1,476	0,140
Lombardo, 2008	0,245	0,284	0,081	-0,311	0,801	0,863	0,388
	0,288	0,139	0,019	0,015	0,560	2,070	0,038

Statistics for each study

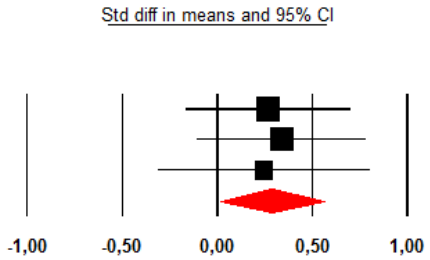

Figure 74: Forest plot for FR 1D:5D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,301	0,178	0,032	-0,048	0,649	1,691	0,091
Manno, 2008	0,259	0,175	0,031	-0,085	0,602	1,477	0,140
Lombardo, 2008	0,301	0,159	0,025	-0,011	0,613	1,890	0,059
	0,288	0,139	0,019	0,015	0,560	2,070	0,038

Std diff in means (95% CI) with study removed

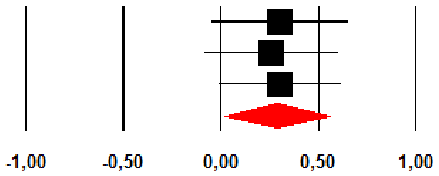

Figure 75: Sensitivity analysis – FR 1D:5D (Fixed-effect model)

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,001	0,221	0,049	-0,433	0,435	0,005	0,996
Manno, 2008	0,337	0,228	0,052	-0,110	0,783	1,476	0,140
Lombardo, 2008	0,450	0,286	0,082	-0,112	1,011	1,570	0,116
	0,231	0,139	0,019	-0,041	0,503	1,664	0,096

Std diff in means and 95% CI

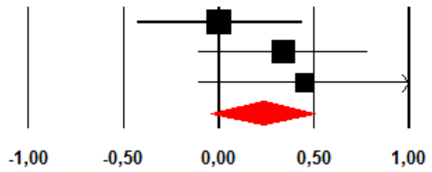

Figure 76: Forest plot for FL 1D:5D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,380	0,178	0,032	0,031	0,730	2,132	0,033
Manno, 2008	0,169	0,175	0,031	-0,174	0,512	0,964	0,335
Lombardo, 2008	0,164	0,159	0,025	-0,148	0,475	1,031	0,302
	0,231	0,139	0,019	-0,041	0,503	1,664	0,096

Std diff in means (95% CI) with study removed

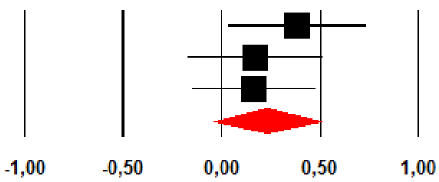

Figure 77: Sensitivity analysis – FL 1D:5D (Fixed-effect model)

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,323	0,224	0,050	-0,117	0,763	1,439	0,150
Manno, 2008	0,187	0,227	0,052	-0,258	0,632	0,825	0,409
Lombardo, 2008	0,151	0,283	0,080	-0,404	0,706	0,533	0,594
	0,231	0,139	0,019	-0,042	0,503	1,658	0,097

Std diff in means and 95% CI

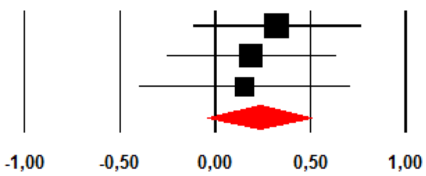

Figure 78: Forest plot for HR 1D:5D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,173	0,177	0,031	-0,174	0,520	0,977	0,328
Manno, 2008	0,257	0,176	0,031	-0,088	0,601	1,459	0,145
Lombardo, 2008	0,256	0,160	0,025	-0,057	0,569	1,603	0,109
	0,231	0,139	0,019	-0,042	0,503	1,658	0,097

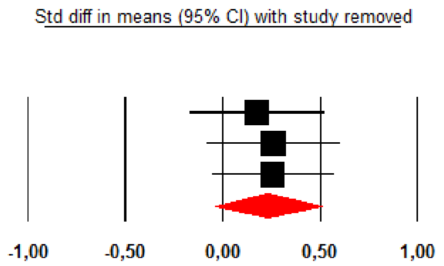

Figure 79: Sensitivity analysis – HR 1D:5D (Fixed-effect model)

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,594	0,228	0,052	0,147	1,041	2,607	0,009
Manno, 2008	0,298	0,228	0,052	-0,148	0,744	1,309	0,191
Lombardo, 2008	0,062	0,283	0,080	-0,493	0,616	0,218	0,827
	0,352	0,140	0,020	0,077	0,626	2,513	0,012

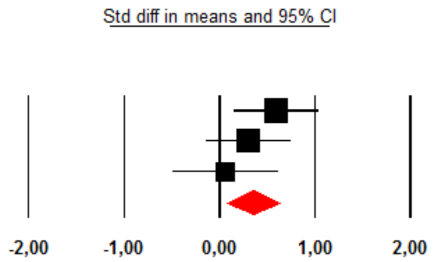

Figure 80: Forest plot for HL 1D:5D (Fixed-effect model)

Study name	Statistics with study removed						
	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
McFadden, 2003	0,205	0,177	0,031	-0,143	0,553	1,156	0,248
Manno, 2008	0,385	0,177	0,031	0,037	0,732	2,167	0,030
Lombardo, 2008	0,446	0,161	0,026	0,130	0,762	2,768	0,006
	0,352	0,140	0,020	0,077	0,626	2,513	0,012

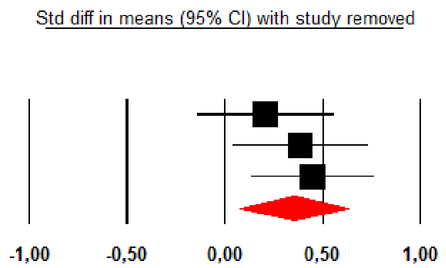

Figure 81: Sensitivity analysis – HL 1D:5D (Fixed-effect model)

7.4. Appendix D

7.4.1. Funnel plots – 2D:4D without bird data

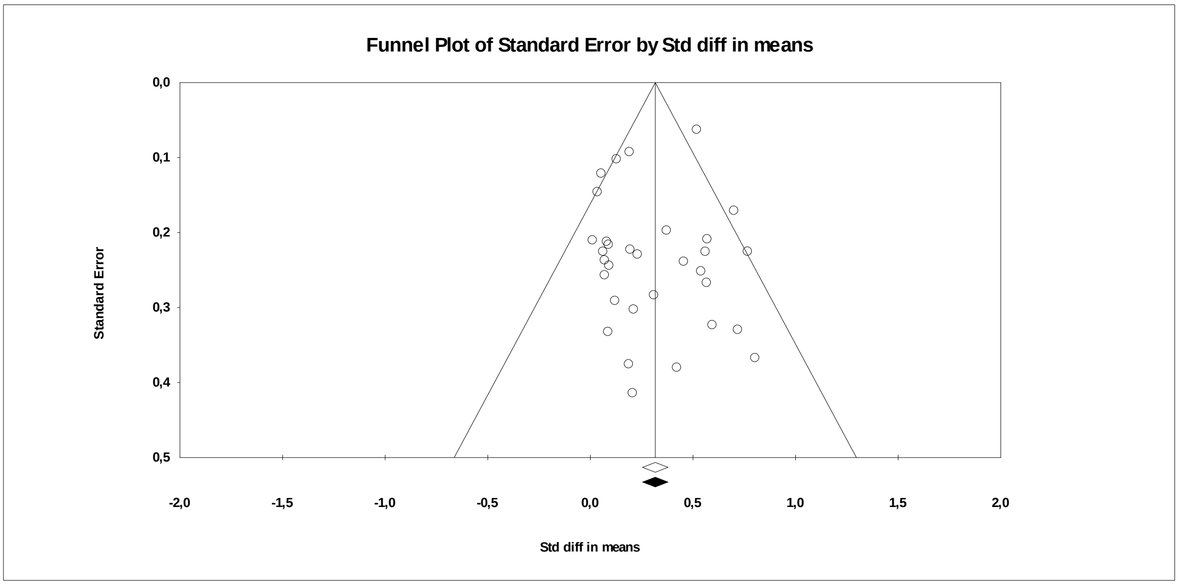

Figure 82: Funnel plot for HR 2D:4D without bird data (Fixed-effect model)

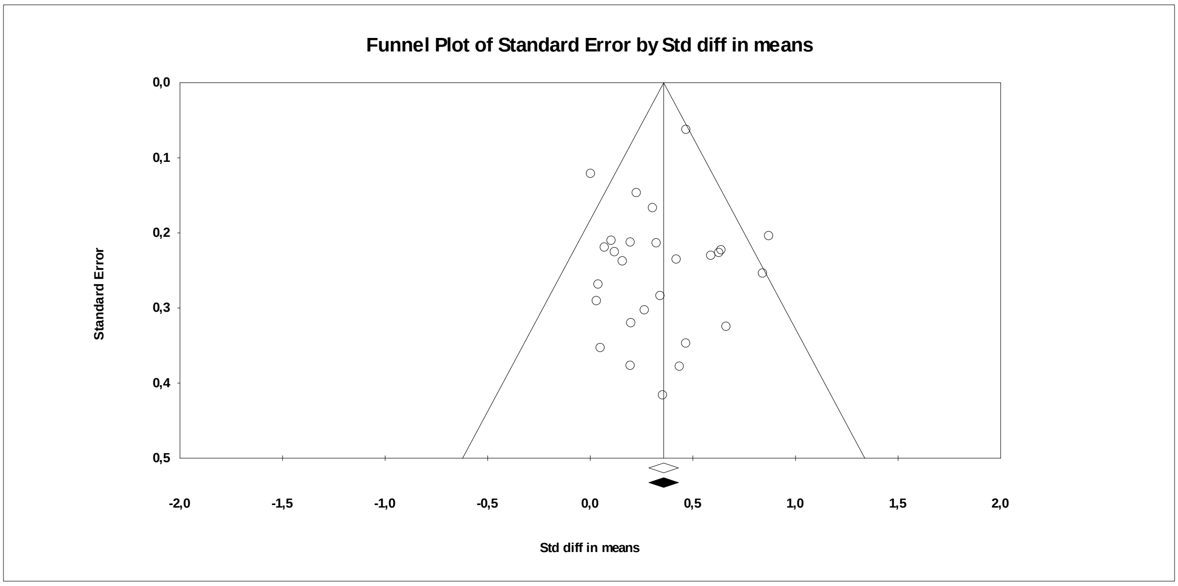

Figure 83: Funnel plot for HL 2D:4D without bird data (Fixed-effect model)

7.4.2. Funnel plots – 2D:3D

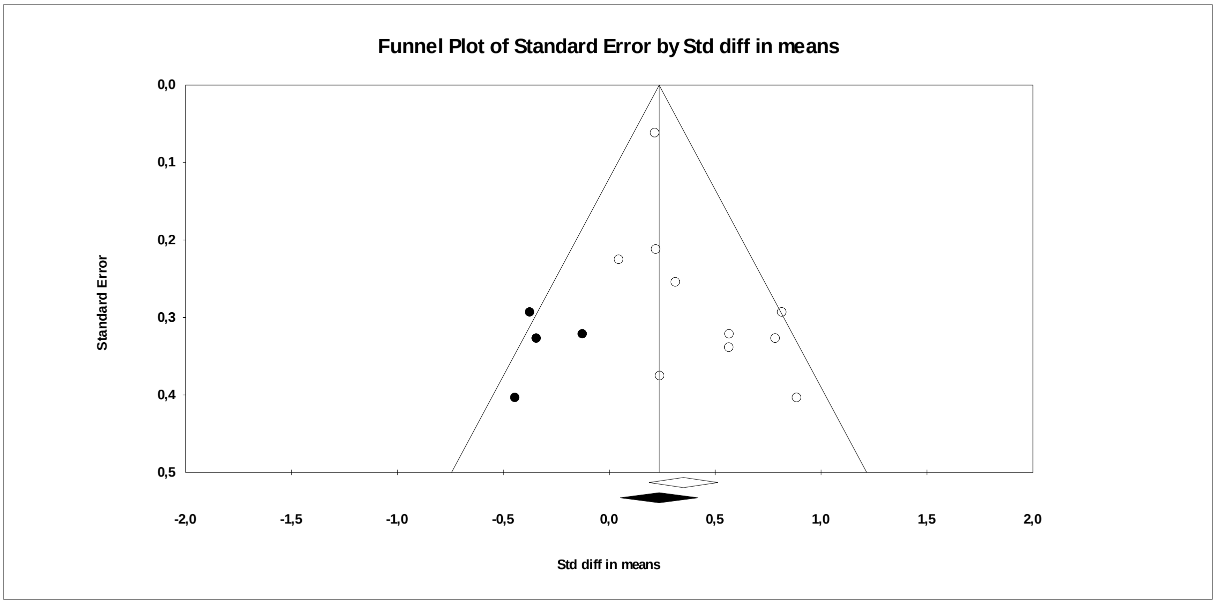

Figure 84: Funnel Plot FR 2D:3D (Fixed-effect model)

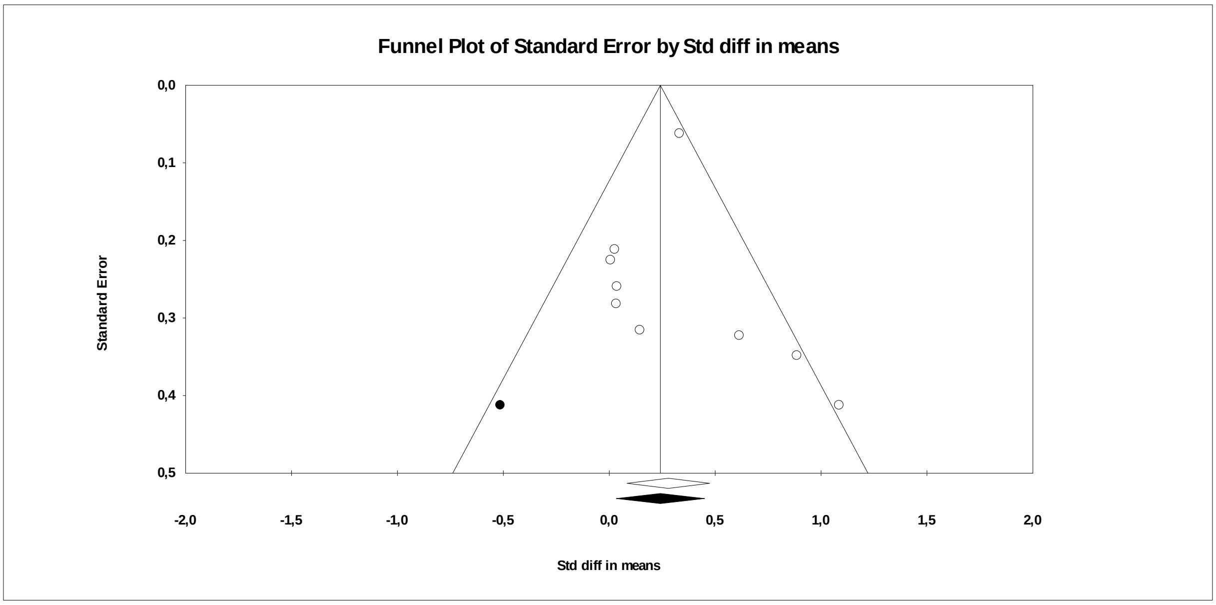

Figure 85: Funnel Plot FL 2D:3D (Fixed-effect model)

Figure 86: Funnel plot HR 2D:3D (Fixed-effect model)

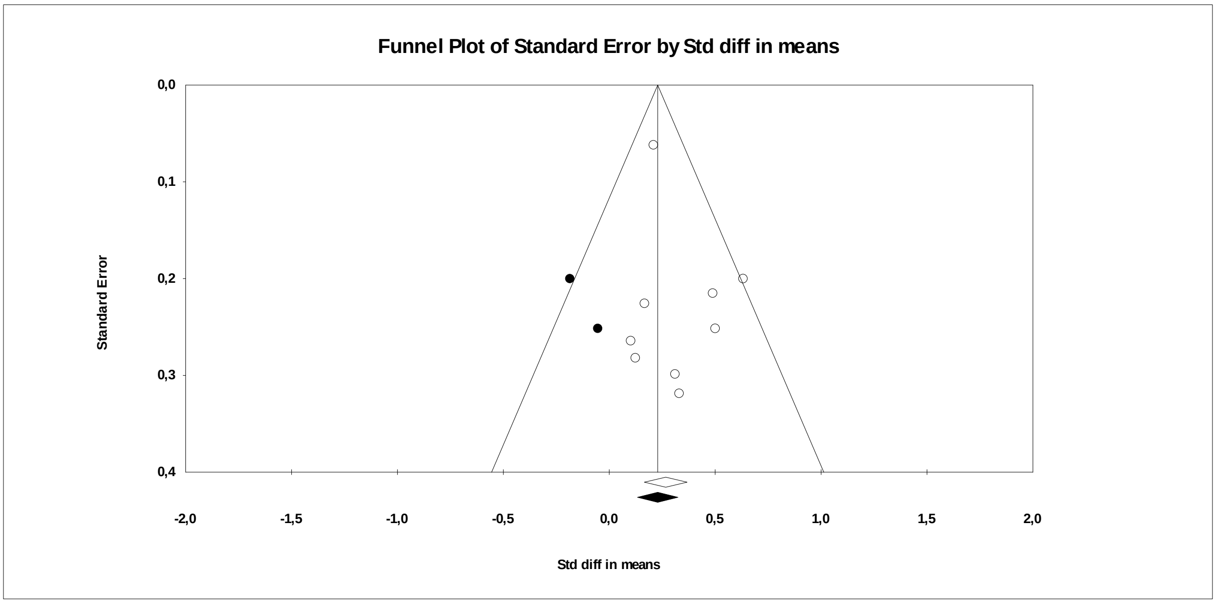

Figure 87: Funnel plot HL 2D:3D (Fixed-effect model)

7.4.3. Funnel plots – 2D:5D

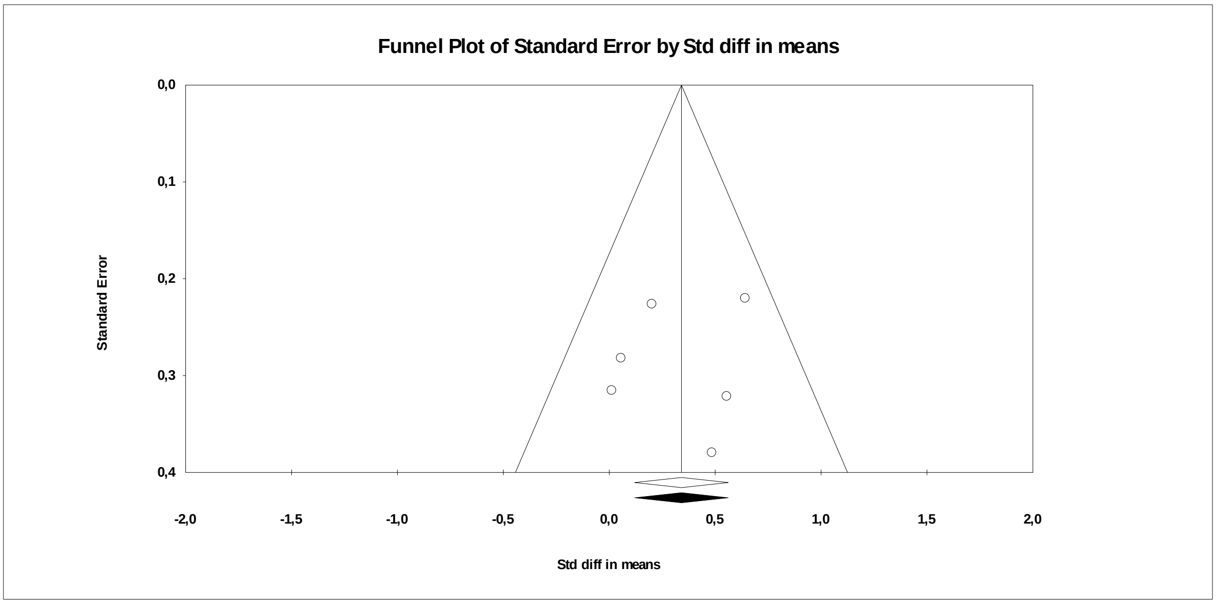

Figure 88: Funnel plot for FR 2D:5D (Fixed-effect model)

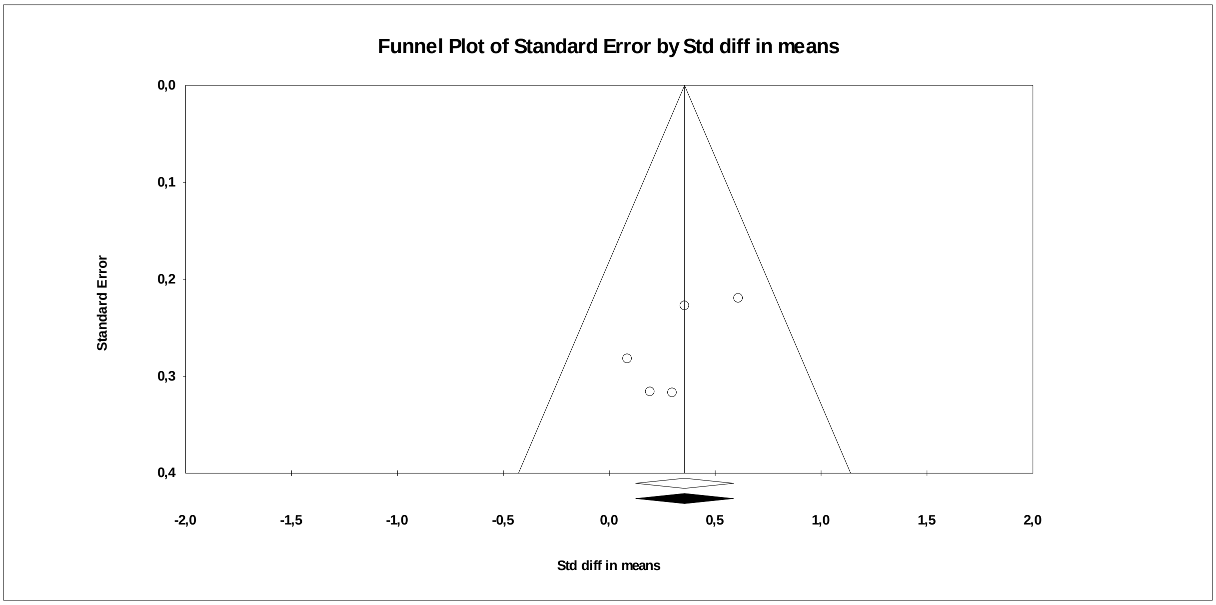

Figure 89: Funnel plot for FL 2D:5D (Fixed-effect model)

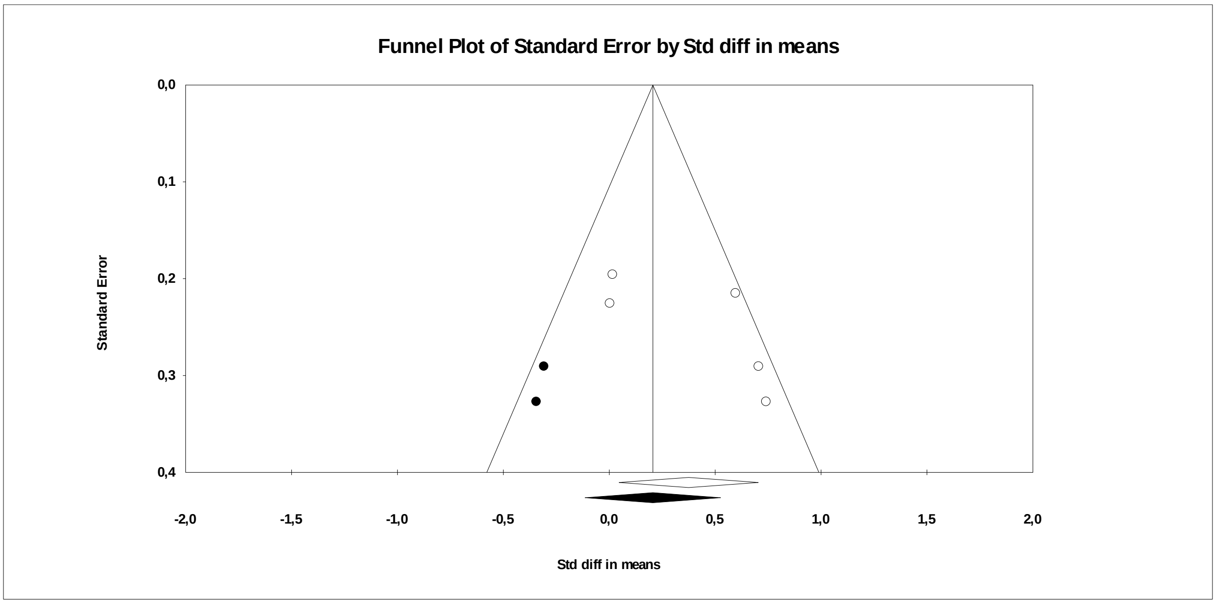

Figure 90: Funnel plot HR 2D:5D (Fixed-effect model)

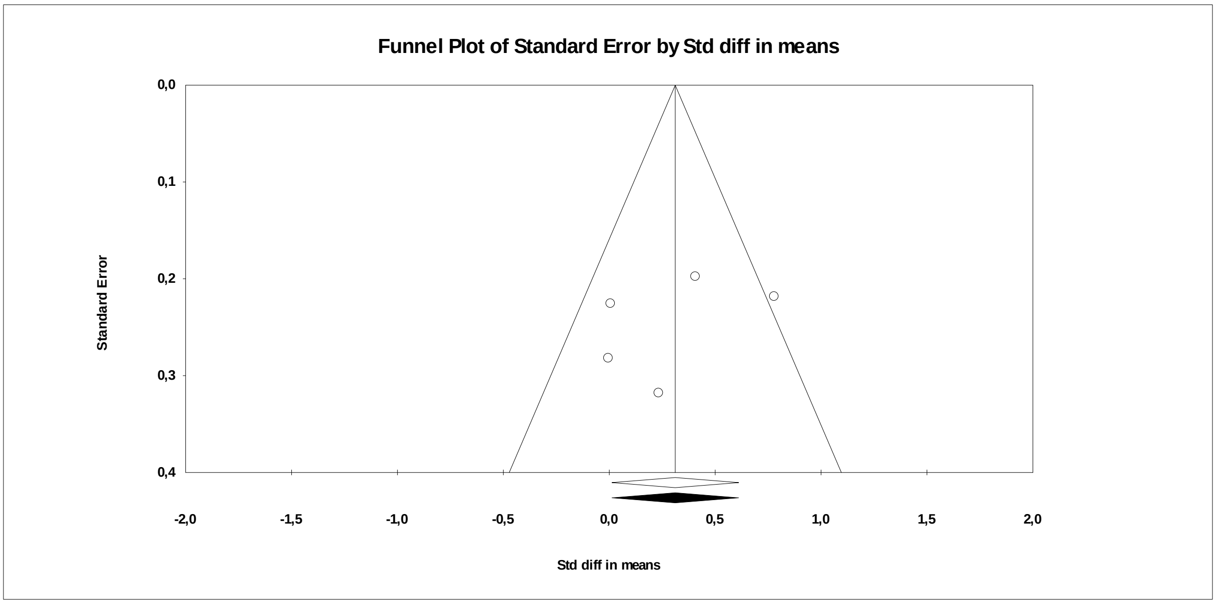

Figure 91: Funnel plot for HL 2D:5D (Fixed-effect model)

7.4.4. *Funnel plots – 3D:4D*

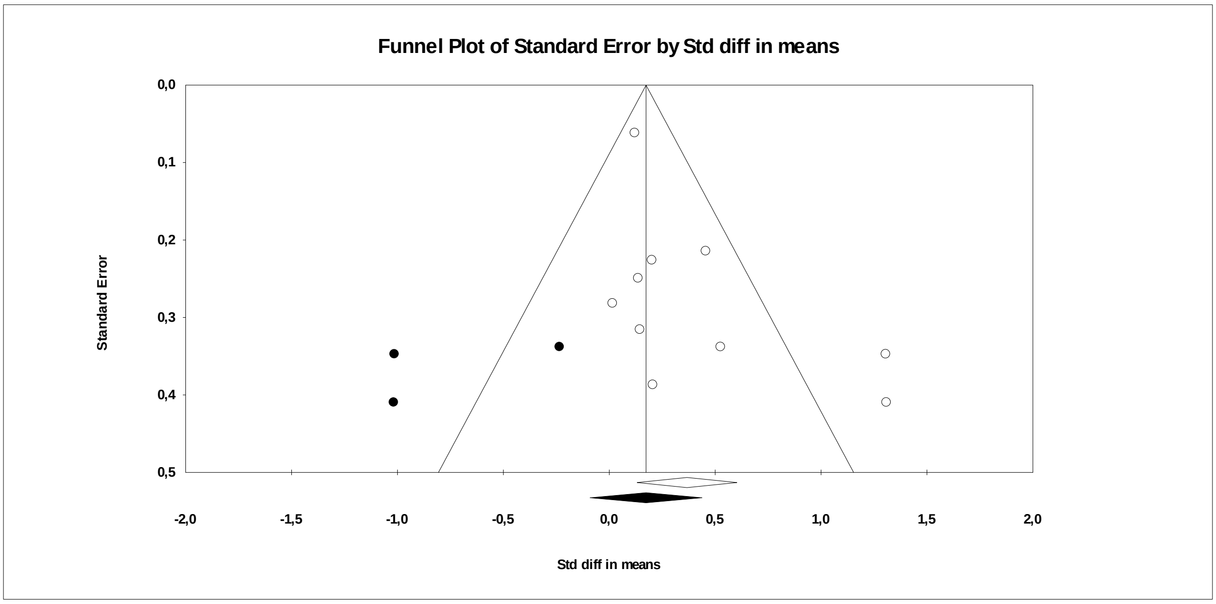

Figure 92: Funnel plot for FR 3D:4D (Fixed-effect model)

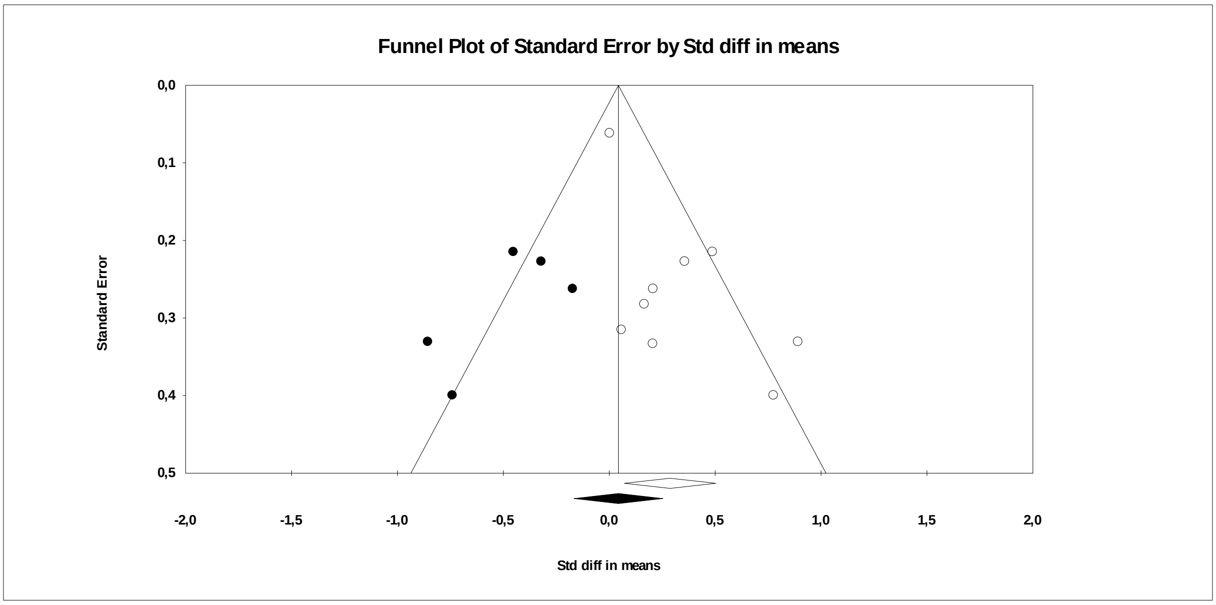

Figure 93: Funnel plot for FL 3D:4D (Fixed-effect model)

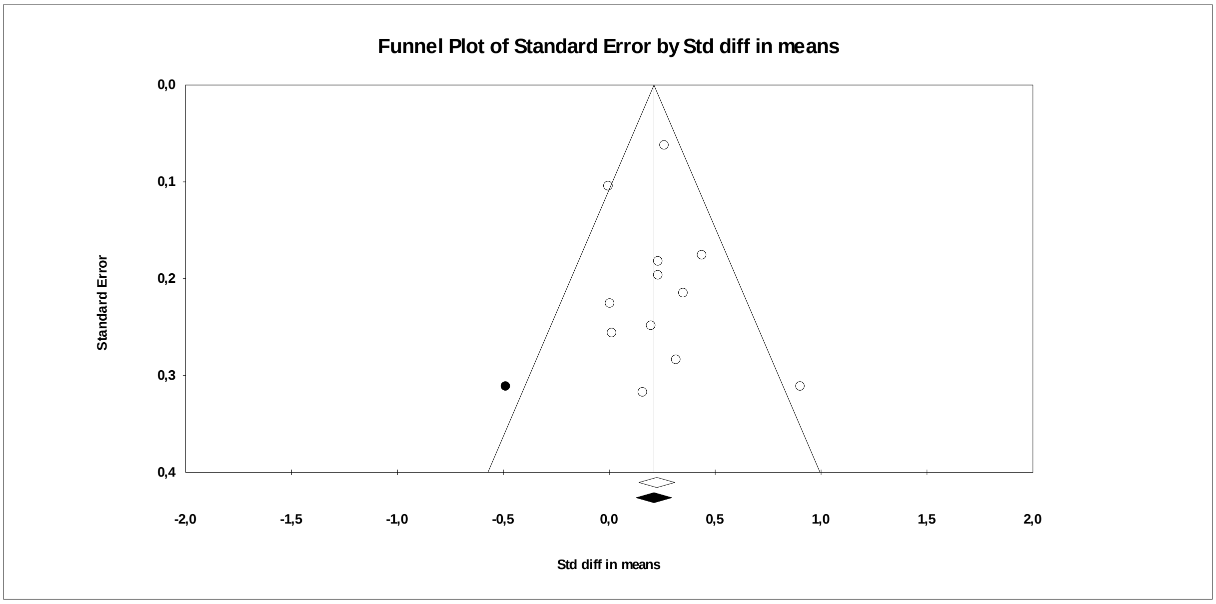

Figure 94: Funnel plot HR 3D:4D (Fixed-effect model)

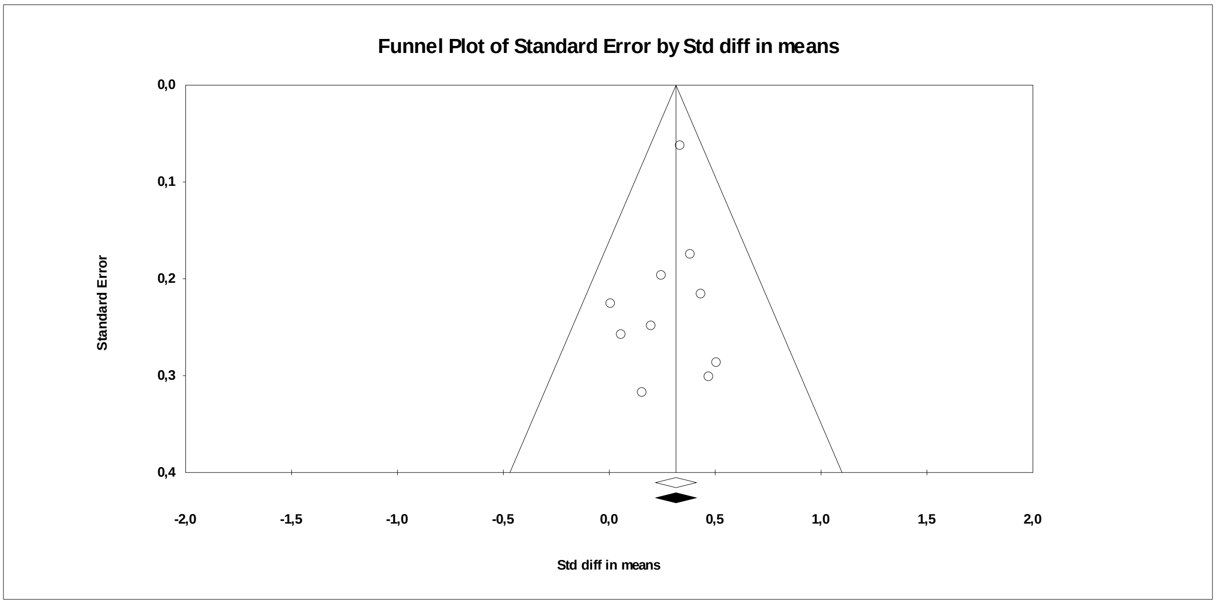

Figure 95: Funnel plot HL 3D:4D (Fixed-effect model)

7.4.5. Funnel plots – 3D:5D

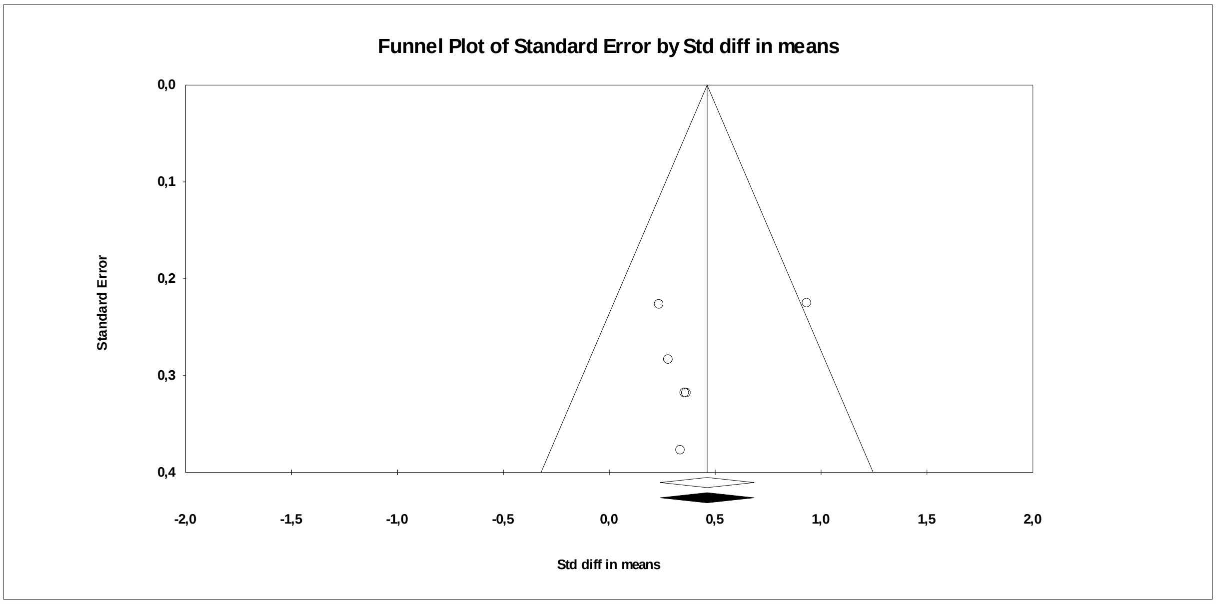

Figure 96: Funnel plot for FR 3D:5D (Fixed-effect model)

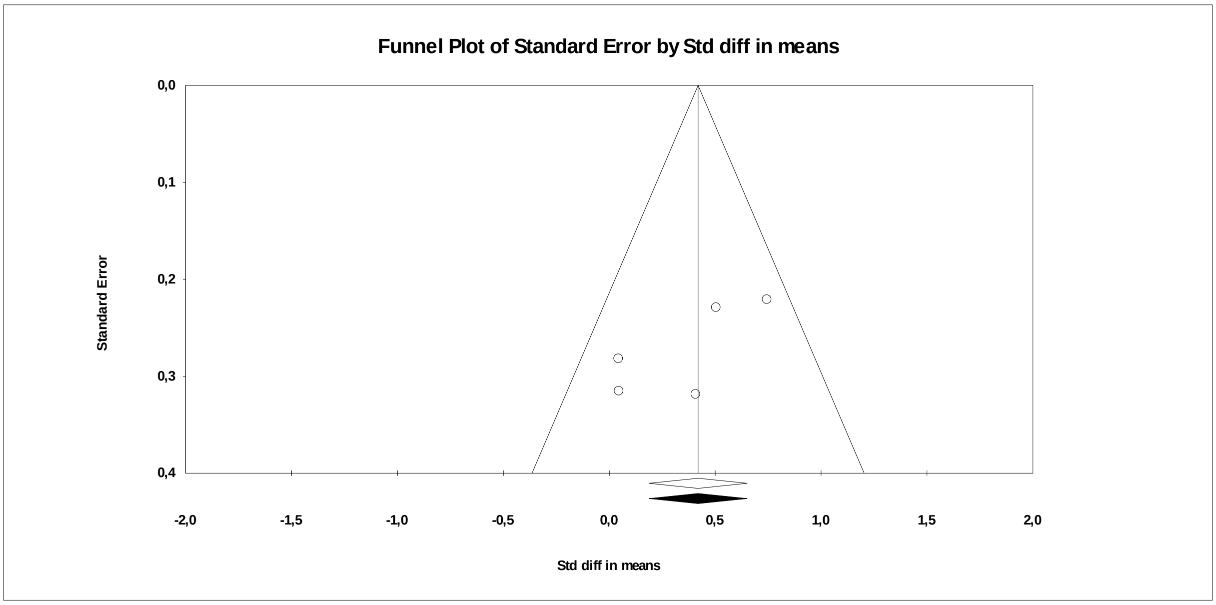

Figure 97: Funnel plot for FL 3D:5D (Fixed-effect model)

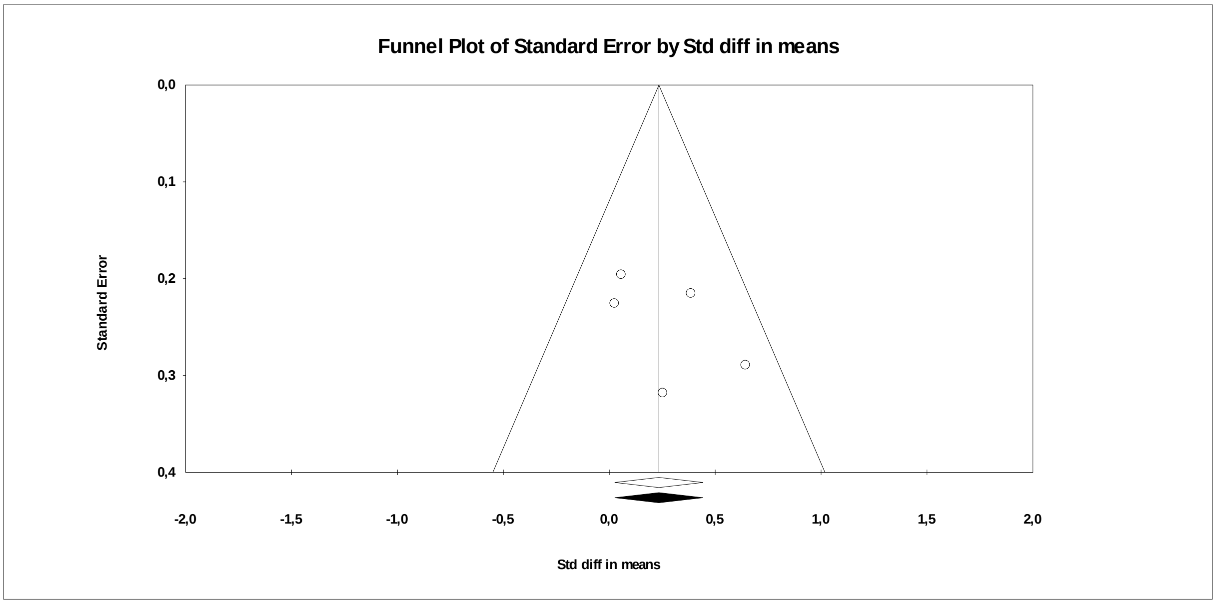

Figure 98: Funnel plot for HR 3D:5D (Fixed-effect model)

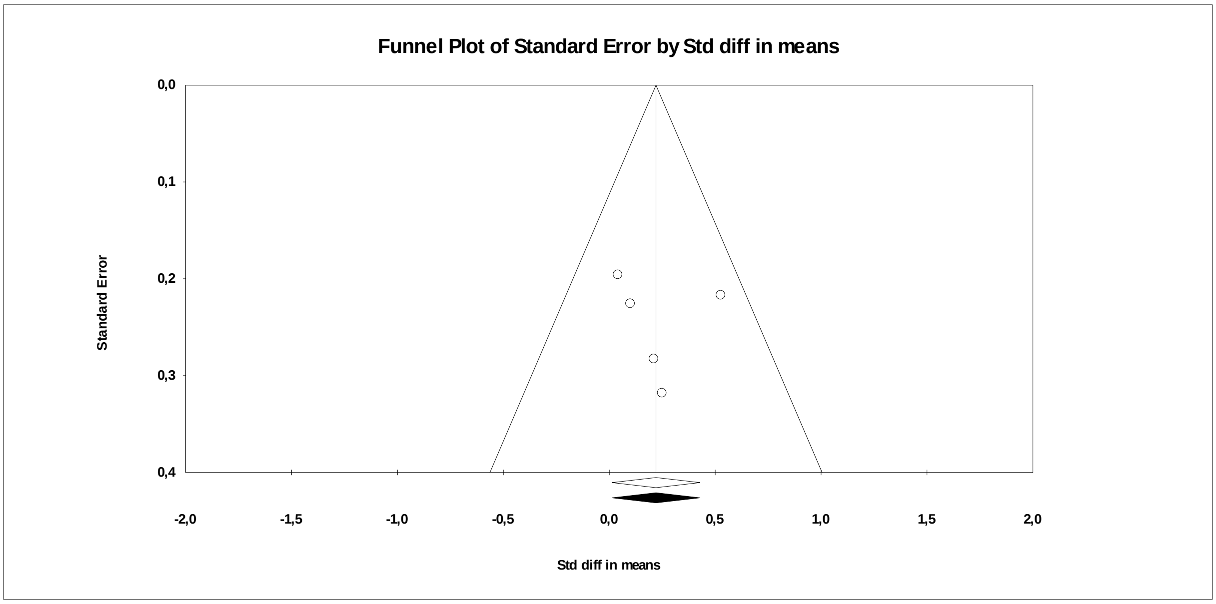

Figure 99: Funnel plot for HL 3D:5D (Fixed-effect model)

7.4.6. Funnel plots – 4D:5D

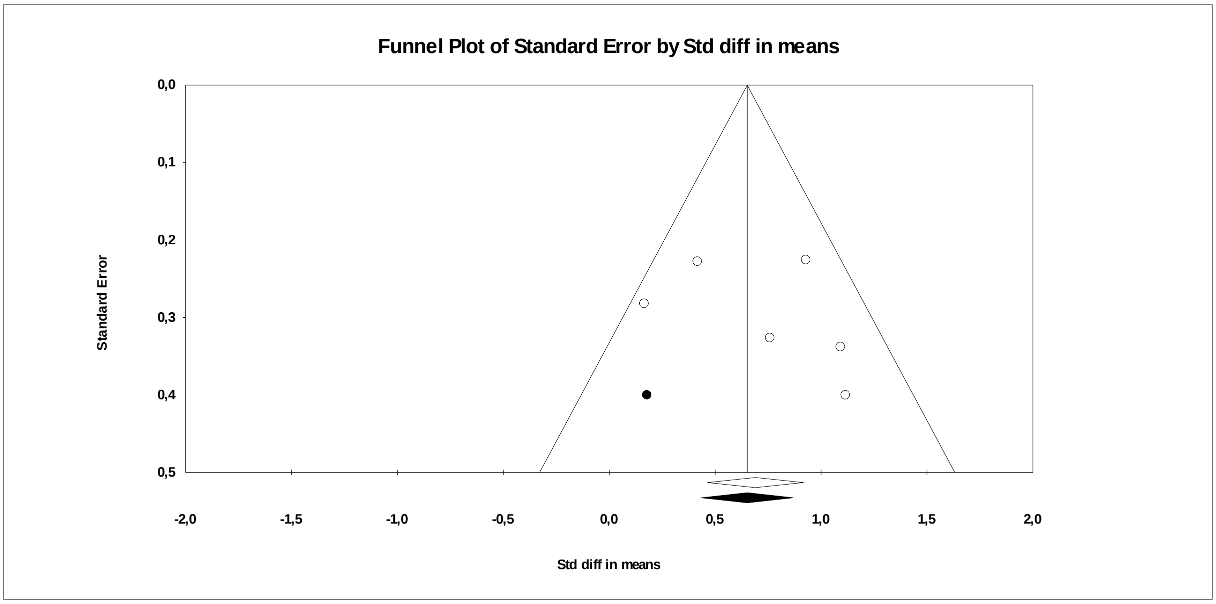

Figure 100: Funnel plot for FR 4D:4D (Fixed-effect model)

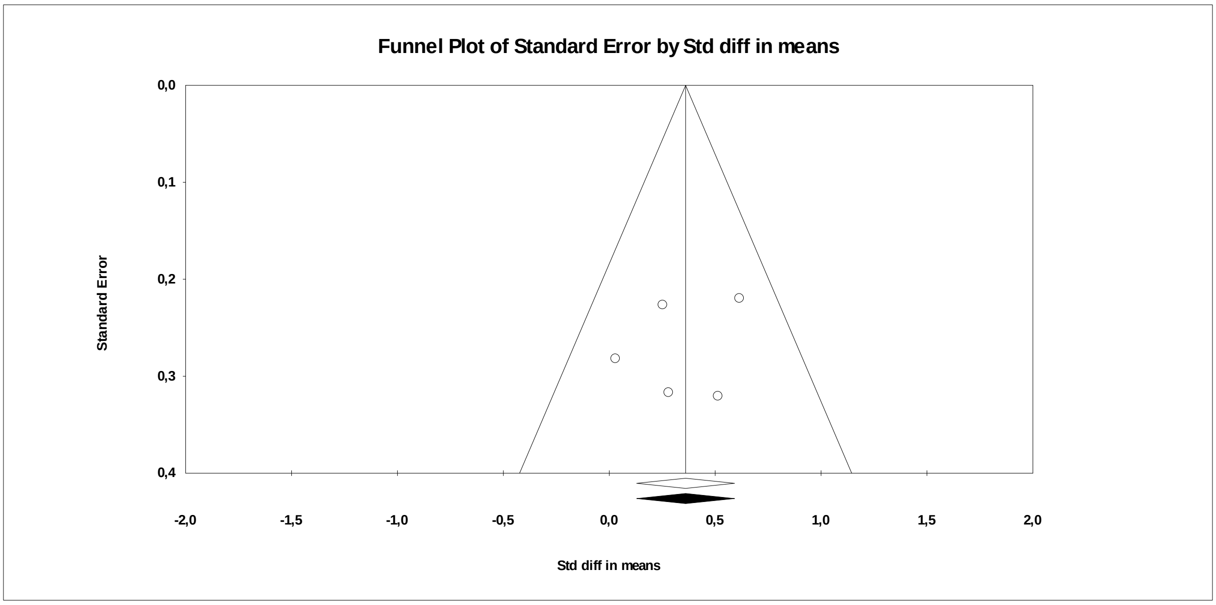

Figure 101: Funnel plot for FL 4D:4D (Fixed-effect model)

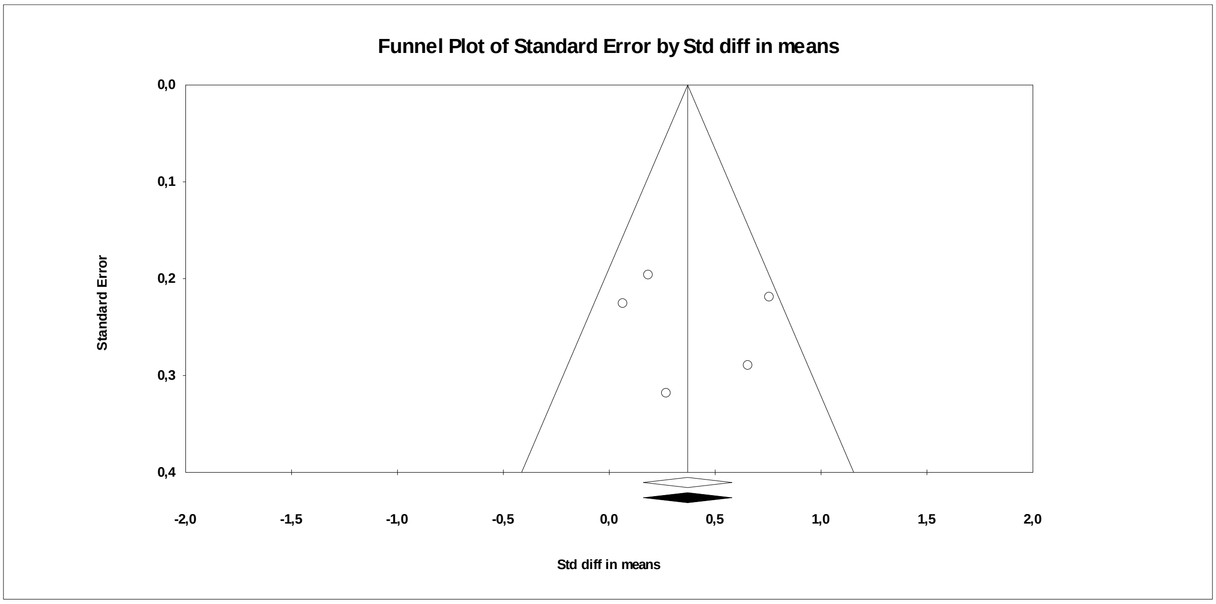

Figure 102: Funnel plot for HR 4D:5D (Fixed-effect model)

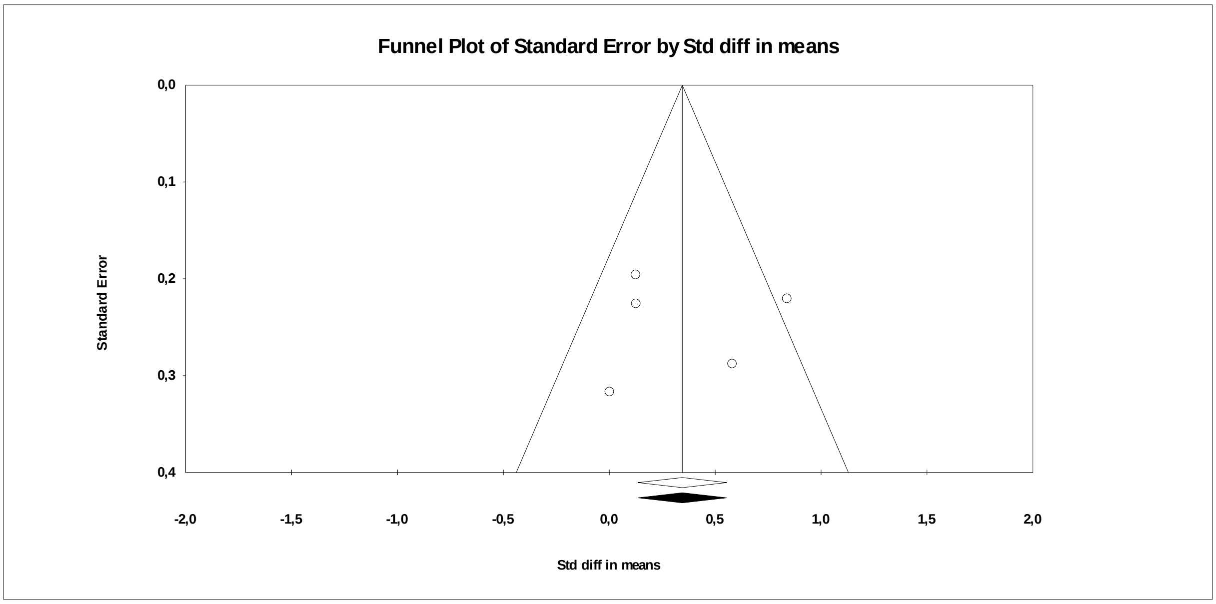

Figure 103: Funnel plot for HL 4D:5D (Fixed-effect model)

7.4.7. Funnel plots – 1D:2D

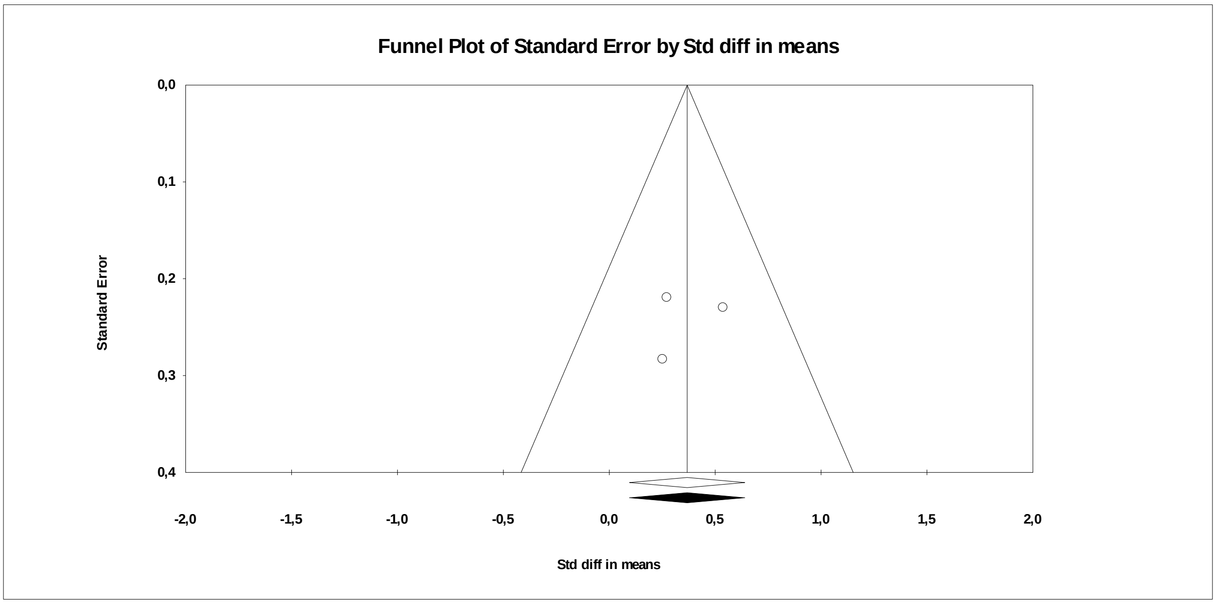

Figure 104: Funnel plot for FR 1D:2D (Fixed-effect model)

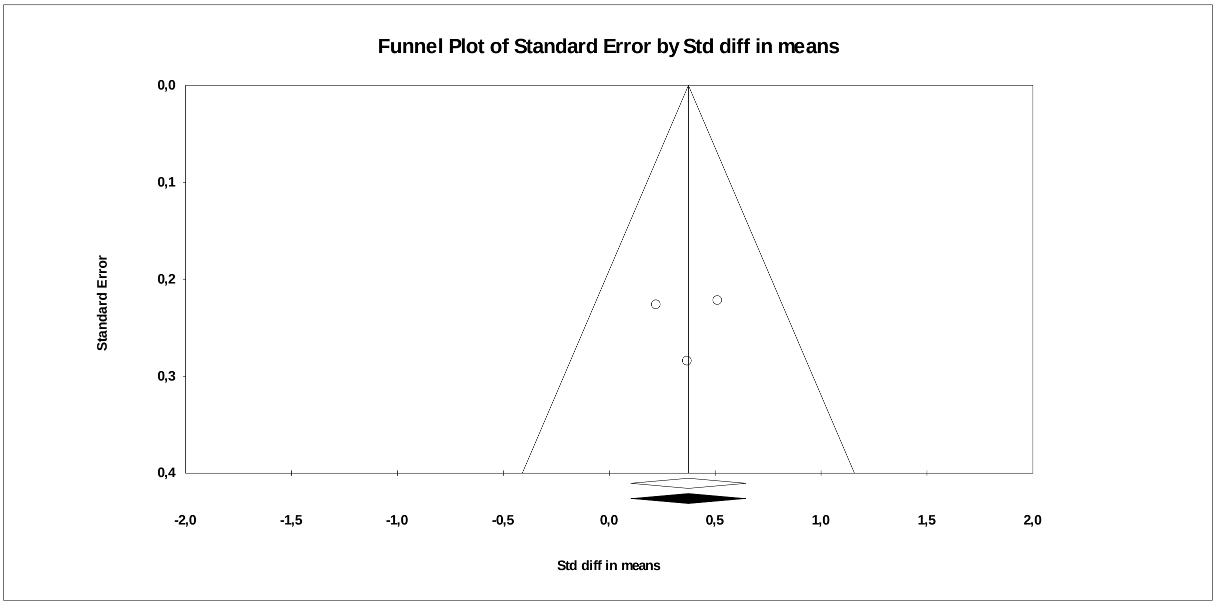

Figure 105: Funnel plot for FL 1D:2D (Fixed-effect model)

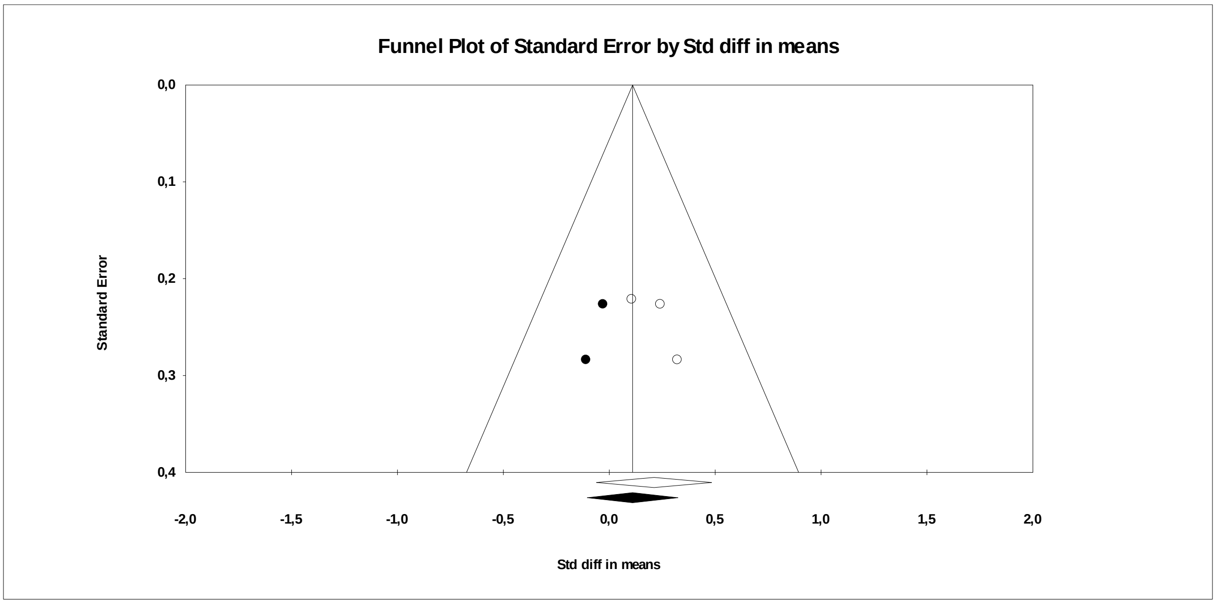

Figure 106: Funnel plot for HR 1D:2D (Fixed-effect model)

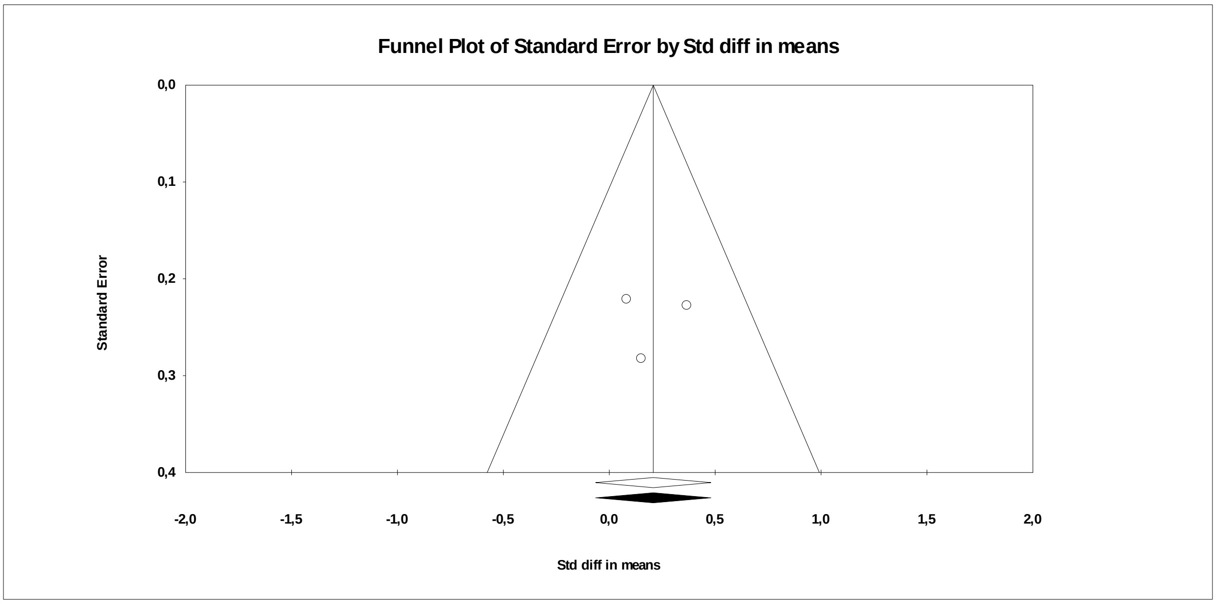

Figure 107: Funnel plot HL 1D:2D

7.4.8. *Funnel plots – 1D:3D*

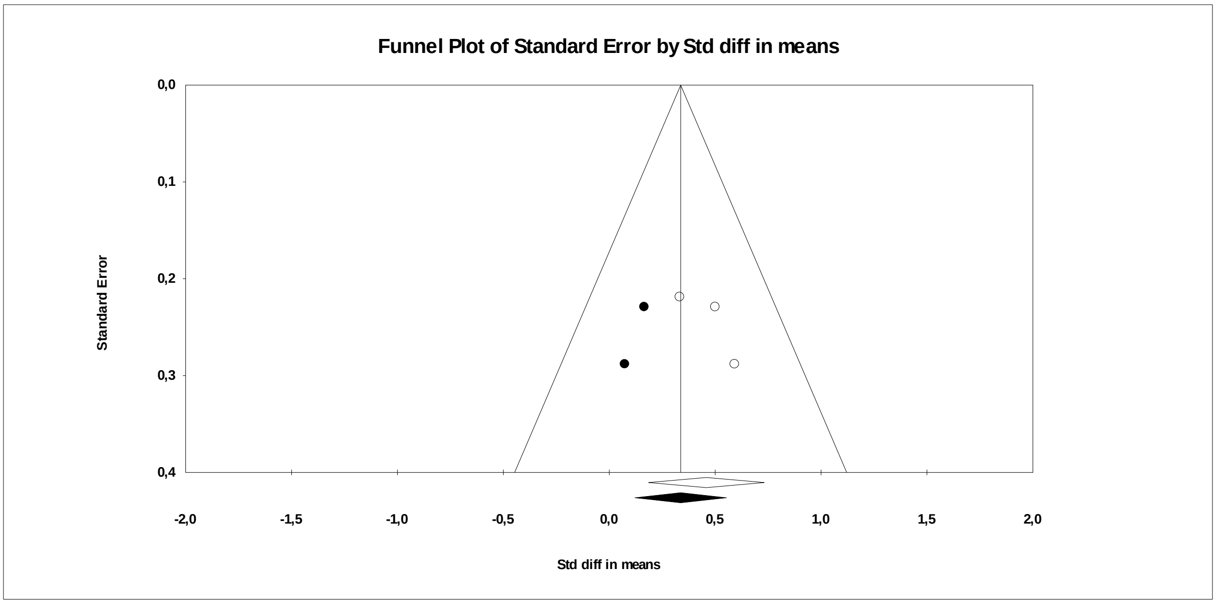

Figure 108: Funnel plot for FR 1D:3D (Fixed-effect model)

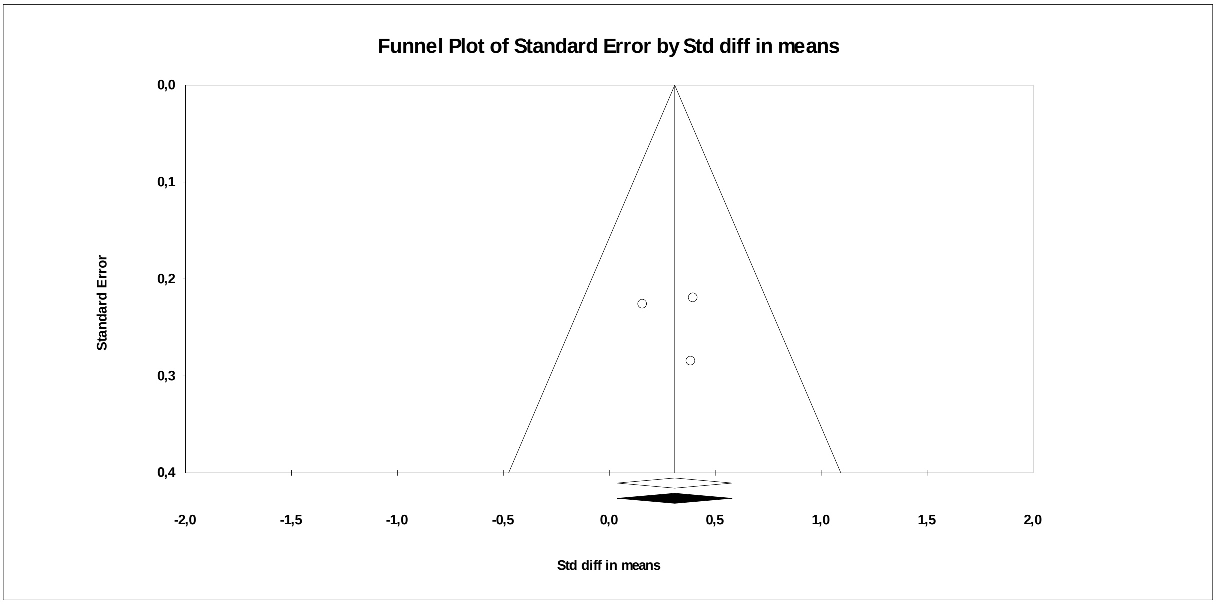

Figure 109: Funnel plot for FL 1D:3D (Fixed-effect model)

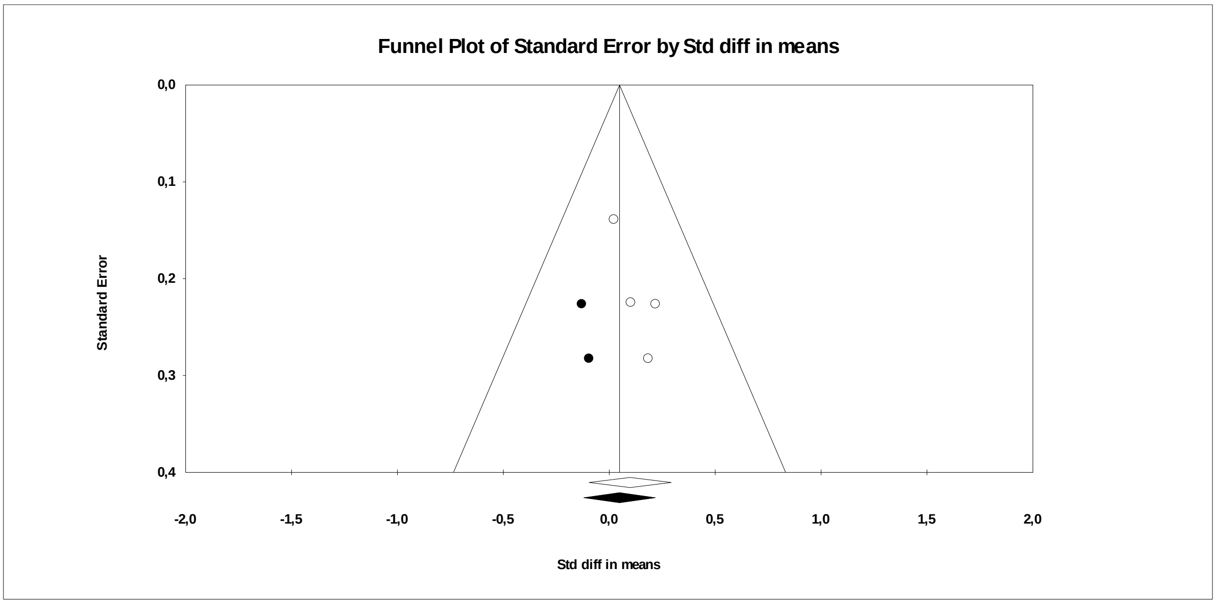

Figure 110: Funnel plot HR 1D:3D (Fixed-effect model)

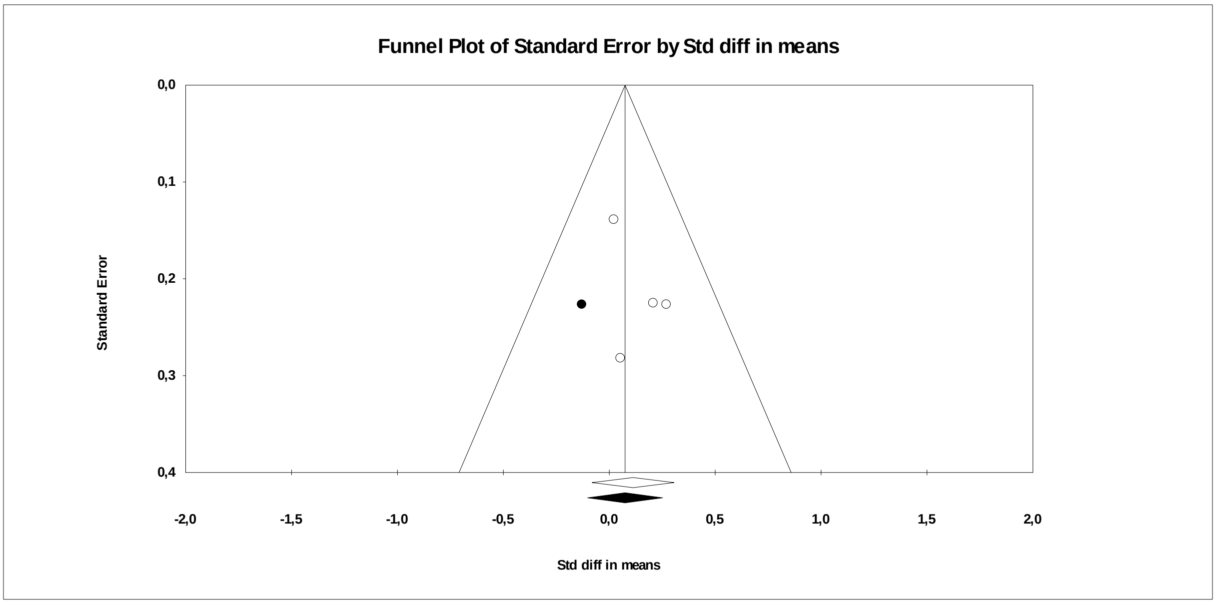

Figure 111: Funnel plot HL 1D:3D (Fixed-effect model)

7.4.9. *Funnel plots – 1D:4D*

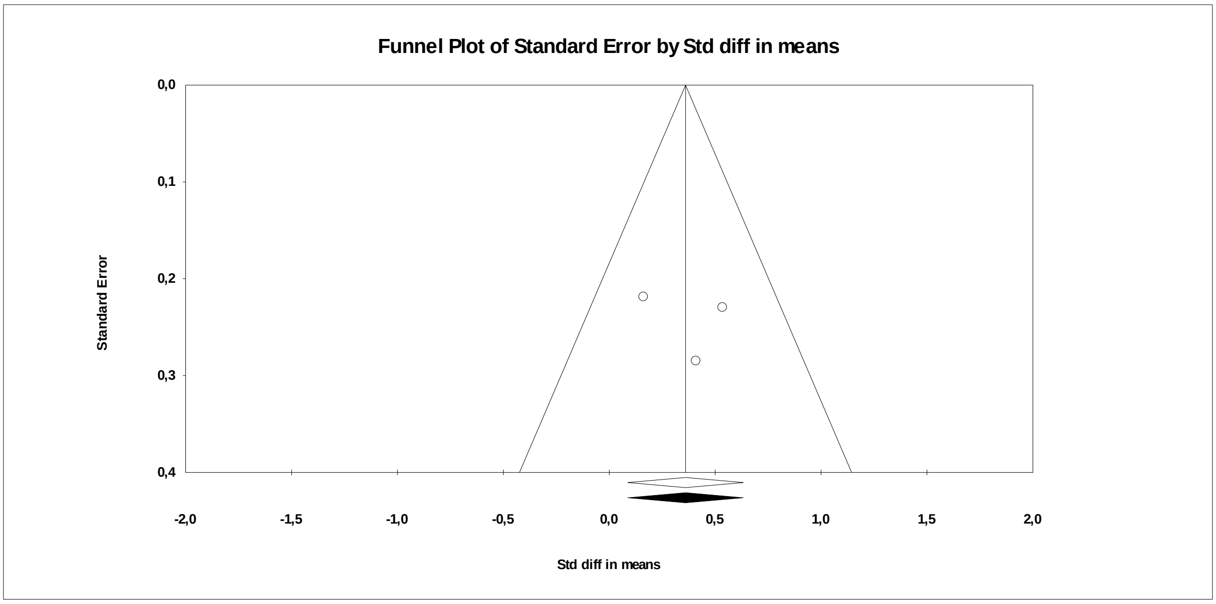

Figure 112: Funnel plot FR 1D:4D (Fixed-effect model)

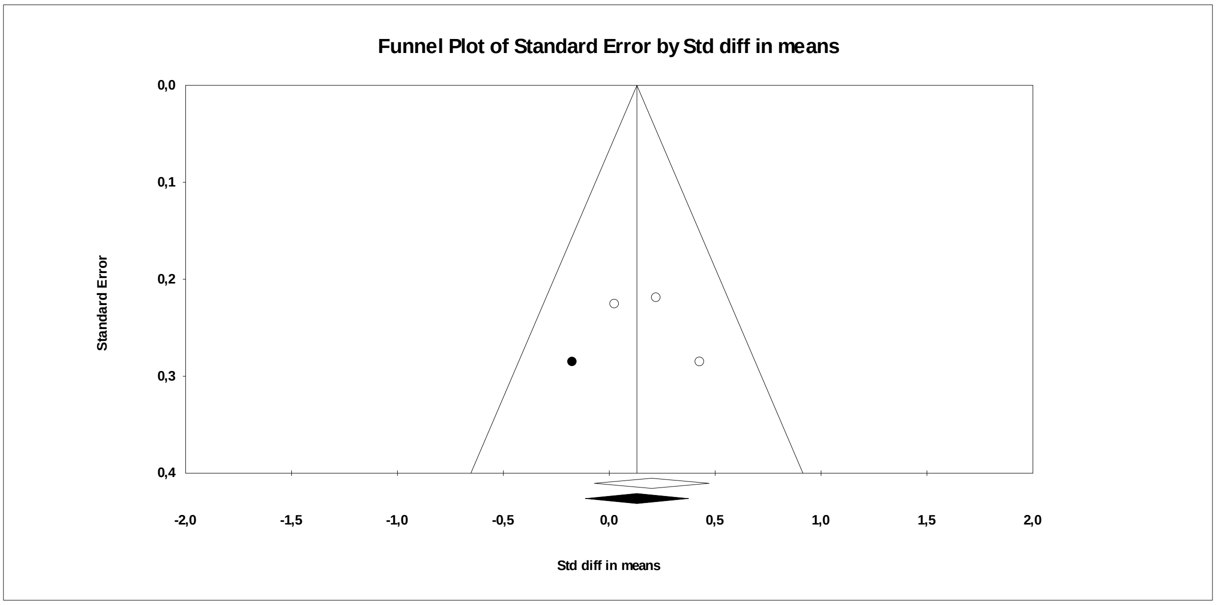

Figure 113: Funnel plot FL 1D:4D (Fixed-effect model)

Figure 114: Funnel plot for HR 1D:4D (Fixed-effect model)

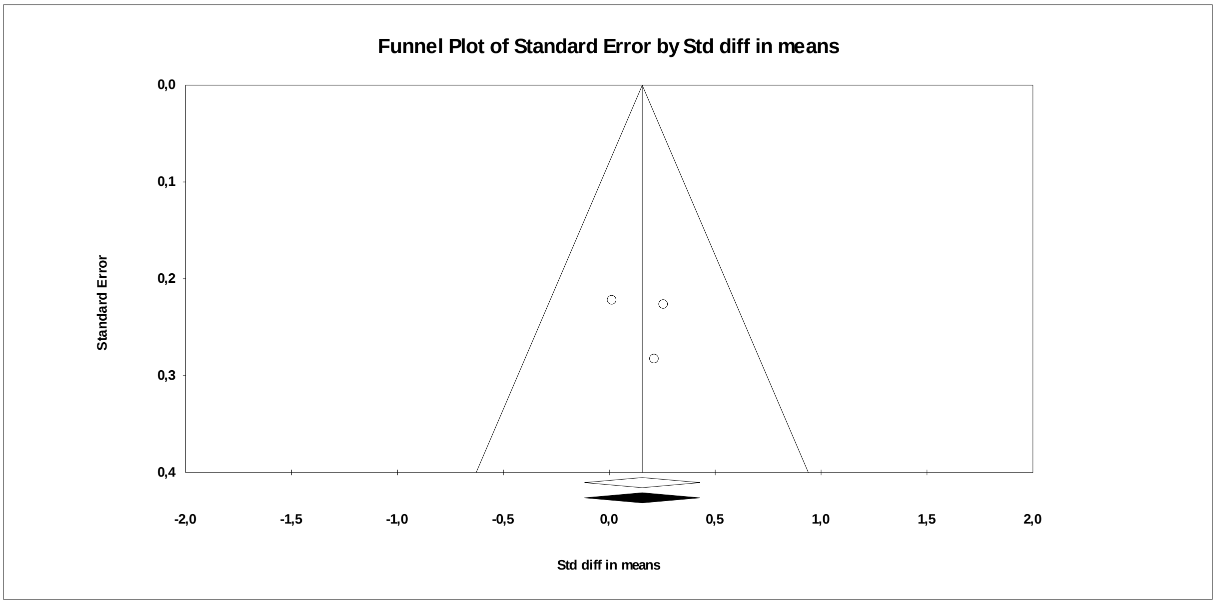

Figure 115: Funnel plot for HL 1D:4D (Fixed-effect model)

7.4.10. Funnel plots – 1D:5D

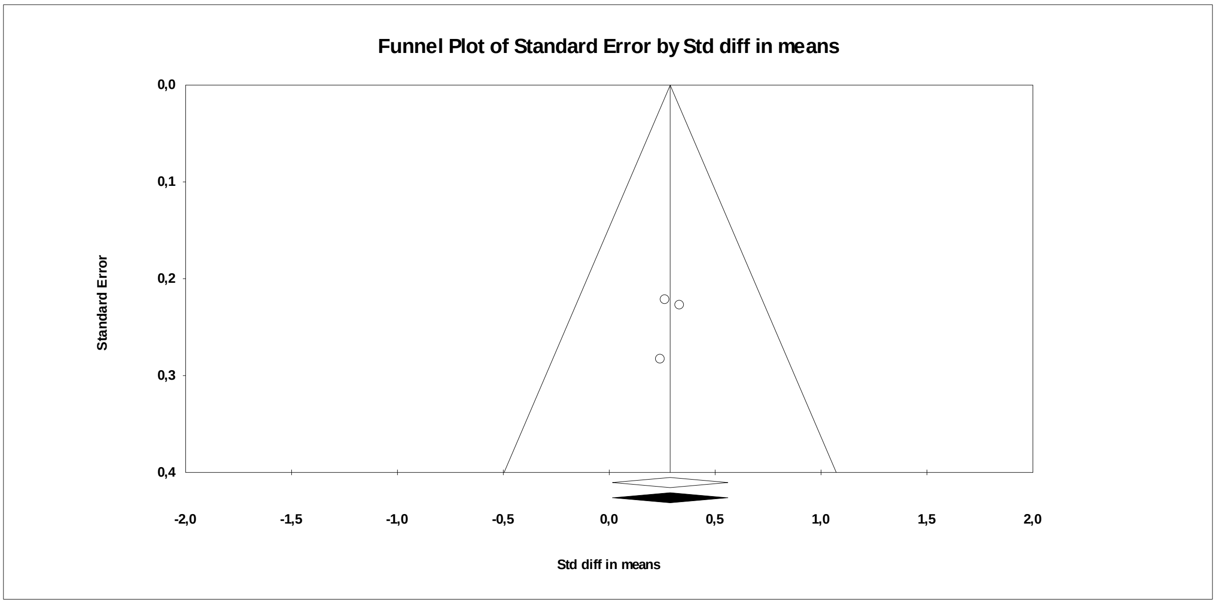

Figure 116: Funnel plot for FR 1D:5D (Fixed-effect model)

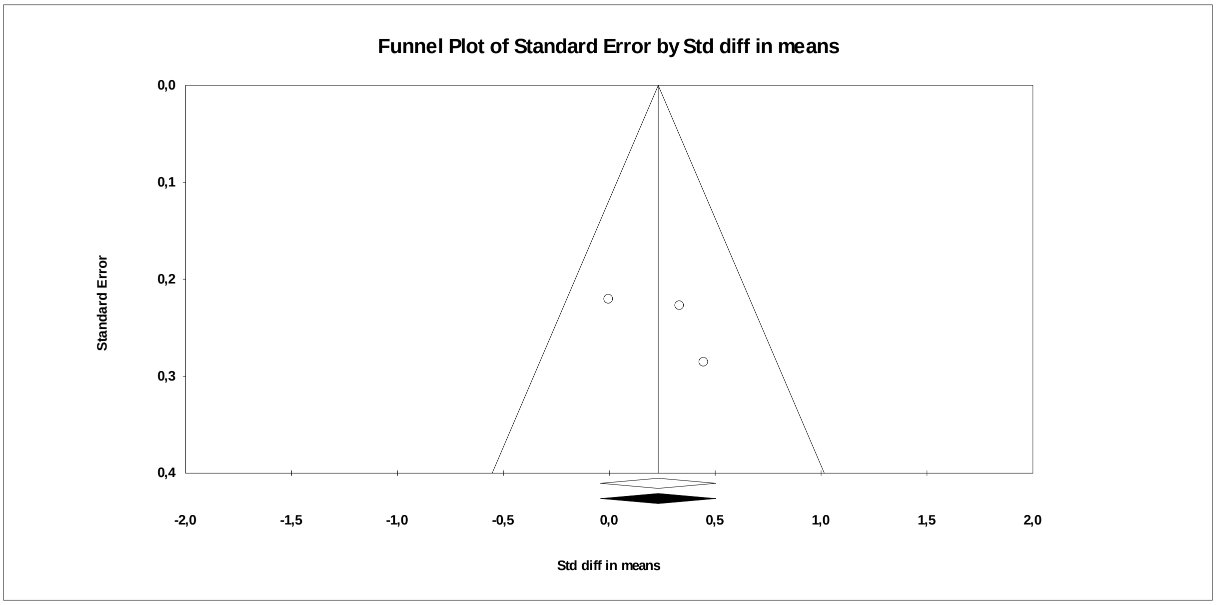

Figure 117: Funnel plot for FL 1D:5D (Fixed-effect model)

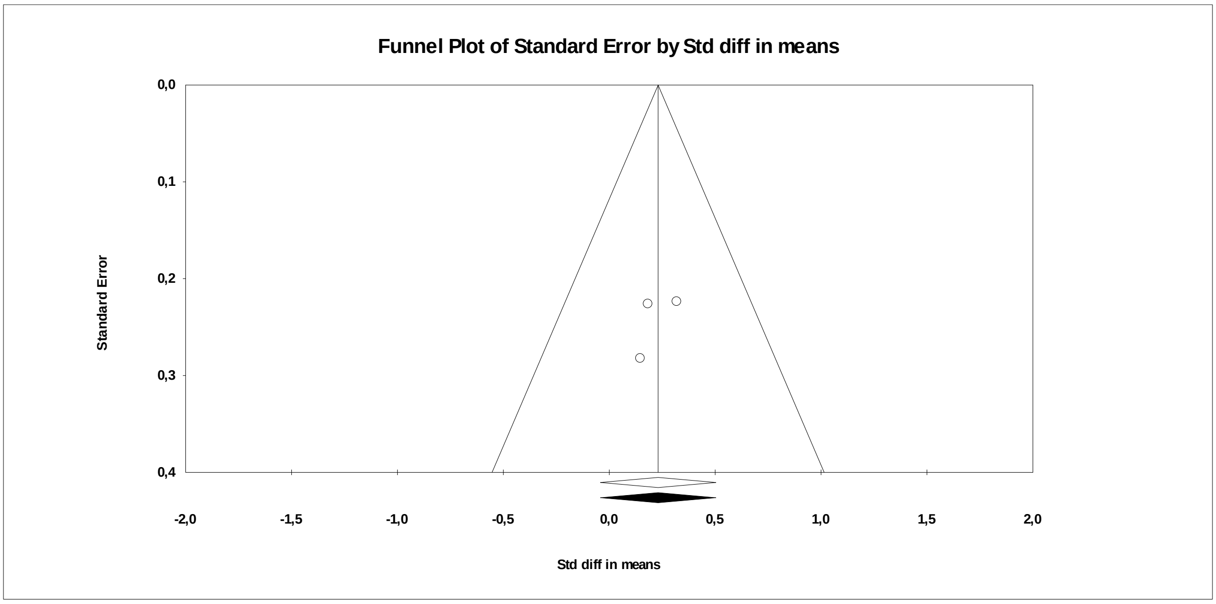

Figure 118: Funnel plot for HR 1D:5D (Fixed-effect model)

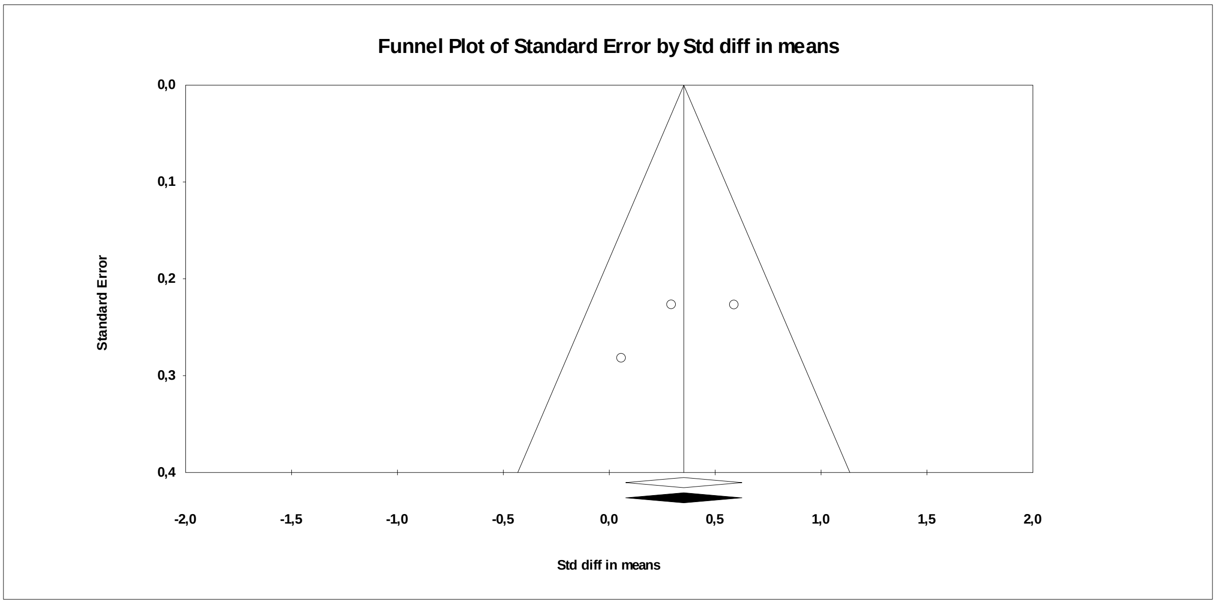

Figure 119: Funnel plot HL 1D:5D (Fixed-effect model)

Eidesstattliche Erklärung

Ich versichere, dass ich die Diplomarbeit selbstständig verfasst, andere als die angegebenen Quellen und Hilfsmittel nicht benutzt und mich auch sonst keiner unerlaubten Hilfe bedient habe.

Ich versichere, dass ich diese Diplomarbeit bisher weder im In- oder Ausland in irgendeiner Form als Prüfungsarbeit vorgelegt habe.

Wien, November 2015

Unterschrift

Curriculum vitae

Persönliche Daten

Name	Rosa Michel
Geburtsdatum	11.02.1986
Geburtsort	Nishnaja Neninka, Altai-Region (Russland)
Familienstand	ledig
Staatsangehörigkeit	Deutschland

Bildungsweg

Seit WS 2008	Studium der Psychologie an der Universität Wien
Seit WS 2010	Studium der Biologie an der Universität Wien
2006 – 2008	Studium der Biologie an der Gutenberg Universität Mainz
1996 - 2005	Gymnasium Traben-Trarbach
1992 - 1996	Grundschule Blankenrath

Berufliche Erfahrung

Seit 2009	Lektorin in der Medienbeobachtung, *Clip Media Service*; Wien

2014	6-wöchiges Praktikum am Institut für Forschungsmethoden der Psychologie, Universität Wien

Ehrenamtliches

2007 - 2008	Hausaufgaben- und Freizeitbetreuung für Kinder und Jugendliche; *Deutscher Kinderschutzbund*, Mainz, Deutschland
Seit 2011	Nachhilfe und Unterstützung der Sprachkompetenz von Kindern, Jugendlichen und Erwachsenen mit Migrationshintergrund, *Kontaktepool*; Wien

Qualifikationen

EDV	MS Office (sehr gut), wissenschaftliche Datenbanken (sehr gut), Comprehensive Meta Analysis (sehr gut)
Sprachen	Englisch fließend in Wort und Schrift, Russisch fließend in Wort und Schrift, Deutsch fließend in Wort und Schrift, Großes Latinum