SYSTEMATIC REVIEW

Dermatoglyphic meta-analysis indicates early epigenetic outcomes & possible implications on genomic zygoty in type-2 diabetes [version 1; peer review: 2 approved]

Seile Yohannes

Department of Biology, College of Natural & Computational Sciences, Jigjiga University, Jigjiga, Ethiopia

V1 First published: 24 Aug 2015, 4:617
<https://doi.org/10.12688/f1000research.6923.1>
 Latest published: 24 Aug 2015, 4:617
<https://doi.org/10.12688/f1000research.6923.1>

Abstract

Background: Dermatoglyphic studies, particularly those arising from the Dutch Hunger Winter Families Cohort, indicate an involvement of prenatal epigenetic insults in type-2 diabetes. However, the exact orchestration of this association is not fully understood. Herein is described a meta-analysis performed based on a belief that such an approach could shed some light as to the role of genetic & epigenetic influences in the etiology of type-2 diabetes.

Methodology/principal findings: The study incorporated reports identified from PubMed, Medline, & Google Scholar databases for eligible case-control studies that assessed dermatoglyphics in type-2 diabetes cases relative to controls. Over 44,000 fingerprints & 2300 palm prints from around 4400 individuals were included in the analysis. Decreased loops patterns [OR= 0.76; 95% CI= (0.59, 0.98)], increased non-loop patterns [OR= 1.31; 95% CI= (1.02, 1.68)], and reduced absolute finger ridge counts [OR= -0.19; 95% CI= (-0.33, -0.04)] were significant findings among the diabetic group. These results are indicative of mild developmental deviances, with epigenetic insults significantly linked to early gestation wherein critical events & signaling pathways of the endocrine pancreas development are witnessed. Further, the increased loop patterns with decreased non-loop patterns were deemed as possible indicators of decreased genomic heterozygosity with concurrently increased homozygosity in the diabetic group, linked to reduced buffering capacities during prenatal development.

Conclusions: Epigenetic insults primarily during the 1st trimester, to a lesser extent between the early-to-mid 2nd trimester, but least likely linked to those beyond the mid-second trimester are evident in type-2 diabetes. It is recommended that future research aimed at expounding the prenatal origins of T2DM, as well as developing novel therapeutic methods, should focus on the early stages of endocrine pancreatic development.

Open Peer Review

Approval Status

	1	2
version 1
24 Aug 2015	view	view

- Buddhika Wijerathne**, Rajarata University of Sri Lanka, Anuradhapura, Sri Lanka
- Tarimobo Ootobo** , University of Toronto, Toronto, Canada
Hospital for Sick Children, Toronto, Canada

Any reports and responses or comments on the article can be found at the end of the article.

Keywords

dermatoglyphics, diabetes, epigenetics, prenatal development, heterozygosity, developmental homeostasis, genetic predisposition

Corresponding author: Seile Yohannes (sygenetix@gmail.com)

Competing interests: The author declares no competing interests.

Grant information: No grants/funding were involved in supporting this work.

Copyright: © 2015 Yohannes S. This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Yohannes S. **Dermatoglyphic meta-analysis indicates early epigenetic outcomes & possible implications on genomic zygoty in type-2 diabetes [version 1; peer review: 2 approved]** F1000Research 2015, 4:617 <https://doi.org/10.12688/f1000research.6923.1>

First published: 24 Aug 2015, 4:617 <https://doi.org/10.12688/f1000research.6923.1>

Introduction

The dawn of the 21st century has witnessed a trend of epidemiologic shift from acute infections to chronic degenerative disorders of intricate etiologies markedly obscure to comprehend. One such multifaceted forerunner deemed as a major global public health issue is diabetes mellitus, recording an estimated global prevalence of 8.3% in 2013 that is projected to rise to an alarming figure of over 590 million afflicted individuals by 2035¹. Type-2 diabetes mellitus (T2DM) accounts for greater than 90% of all diabetics². It is a polygenic multi-factorial disorder entailing multiple endogenous & exogenous risk factors^{3,4}.

The estimated heritability of T2DM underscores the contribution of non-genetic components in its etiologic complexity⁵. Several prenatal environmental agents have been hypothesized as putative risk factors for T2DM, including: maternal dietary patterns, objective hardship or stress related to natural disasters, season of birth (related to vitamin D or melatonin metabolisms), urbanization, medications such as corticosteroids during pregnancy, use of pesticides, and so on^{6–10}.

In line with this, the Dutch Hunger Winter Families Cohort studies investigate the concept of the *thrifty phenotype hypothesis*, linking gestational hunger to the offspring's adulthood insulin resistance, glucose intolerance, and subsequent development of diabetes^{11,12}. Such outcomes have in turn been shown to be associated with epigenetic alterations, including changes in the normal pattern of DNA methylation among genes essential for growth & development^{4,13–15}. Yet, further studies from varied populations originating from varied environmental settings are necessitated in order to comprehend such etiologic complexity.

A currently emerging area of study with multifarious findings of peculiar phenotypes among a broad array of chronic disorders including T2DM is dermatoglyphics (DG). It refers to the systematic study of the friction ridge features on the palmar & plantar surfaces, which are formed as complex polygenic multi-factorial traits^{16,17}.

Development of DG begins during the 6th week of gestation, and their basic structure remains unaffected by subsequent environmental insults following full establishment during the 24th week¹⁸. Owing to this & several other advantageous features of DG, prospects of serving as markers to explore the nature & timing of intra-uterine irregularities have been assessed¹⁹. Developmental noise associated with chromosomal/gene abnormalities, environmental pressures, or a combination of these, have been shown to be detectable via DG²⁰.

Despite their pervasiveness, studies exploring DG in T2DM that entail strong deductions fortified by models that elucidate the underlying developmental mechanism in play thereby vindicating such associations, are distinctively vague. The manifold DG variable types, methodological discrepancies, as well as poorly designed or implemented studies have been deemed citable attributes to the prevalent contradicting findings²¹.

In contrast, a momentous cluster of researchers stand-out from among this crowd, which view peculiar DG as ripple-effects of early prenatal insults behind the structural & functional defects intrinsic of T2DM *per se*, including pancreatic endocrine system (β -cell functioning) alterations^{22–26}. Though the core of such studies contends that DG are indicative of possible genetic predispositions or epigenetic prenatal outcomes, the exact orchestration of this association is not fully understood. This impedes the strides in the etiological understanding of T2DM, rendering the concept of employability of DG in genetic epidemiology to still be subject to further debate & research.

Herein is described an exhaustive meta-analysis based on a hypothesis that an advanced statistical approach would lead to better conclusive results that will shed some light as to the role of genetic & epigenetic influences in the etiology of T2DM.

Methods

The protocols for this work adhered to the principles of the Cochrane's guidelines for systematic reviews²⁷, as well as the preferred reporting items for systematic reviews and meta-analyses 'PRISMA'²⁸. The PRISMA checklist of the study is depicted in [Supplementary file S1](#).

Criteria for considering studies for this review

A literature search of studies published up to July 2015 which report the association between diabetes and dermatoglyphics was performed, wherein PubMed, PubMed Central, Medline, & Google Scholar databases were exhaustively searched using synonyms and combinations of the terms, as summarized in [Table 1](#). As a secondary option, reference lists of initially identified studies were hand-searched for putative studies, which were, once identified, looked up in the archives of journals they were published in. The data search was performed three times to ensure exhaustiveness, twice before the analysis, and a final cross-checking search after the analysis was completed based on the studies identified from the two initial searches.

Table 1. Search term combinations used to identify putative studies reporting dermatoglyphics in T2DM.

Search Term 1	Search Term 2
"Diabetes" Or 'insulin resistance'	"Dermatoglyphics" Or "Friction ridges"
	'fingerprint' Or "Arch, Loop, Whorl"
	"palm print"
	"atd"
	'ridge count' Or "TFRC, AFRC, ARC, a-b, a-d, b-c, c-d"

The eligibility of each of the studies strictly adhered to the following criteria: (1) the article reports on an original peer-reviewed analysis; (2) it is available as a full text article published in English; (3) the article includes relevant raw data for pair-wise comparisons, mainly odds ratios (OR), confidence intervals (CI), mean values, and standard deviations (SD), or at least reported sufficient data that can be employed to estimate these parameters, including count or frequency data, accurate percentage frequencies, or standard errors of mean values.

For studies with some missing raw data or manifesting some inconsistencies hindering accurate extraction of data for meta-analysis, an attempt was made to contact the authors, which was done twice for each corresponding author within a 30 day interval via email addresses available on their articles. Data from responsive authors within the 30 days from the second contact (60 days in total) were included in the analysis.

Dermatoglyphic measures

The continuous dermatoglyphic variables included by a recent dermatoglyphic meta-analysis on schizophrenia were adopted²⁹, and included herein in addition to a few more relevant continuous variables, as well as the inclusion of dichotomous type variables (pattern type distribution).

Thereby, three major classes of variables, each with respective subclasses, were included: Fingerprint patterns: based on the three pattern classification of fingerprint patterns as: arch, loop, and whorl patterns. Ridge counts: a count of ridges between a triradius and a core (in fingerprint patterns), or between two triradii (for palmar ridge counts). Thus the total finger ridge count (TFRC), absolute finger ridge count (AFRC), and total palmar a-b ridge count (TABRC) were assessed. Palmar Angles: angles formed by joining distal palmar inter-digital triradii a/d with the proximal palmar axial triradii t, yielding the ATD, DAT, and ADT angles^{30,31}.

Data extraction & summary

Qualitative and quantitative DG variables reported by each study were extracted carefully and summarized in coded spreadsheets. Pattern frequencies or means and SDs were pooled from left- & right-hand data, as well as from male and female data for each study as per previous reports²⁹. Whenever necessary, percentage frequencies were converted to counts, and SDs calculated from reported standard error of means by multiplying standard errors of means from within a treatment group by the square root of the sample size²⁷.

Statistical analysis

Cochrane RevMan 5.3³² & MetaXL 2.2 software were used for analyses. Hedge's *g* effect sizes for each continuous variable & ORs for each dichotomous variable, together with respective 95% confidence intervals, *z*-scores, & *p*-values were estimated²⁷.

Heterogeneity across studies was assessed following the I^2 statistics³³. The pooled effect size estimations were done using the fixed-effect model if heterogeneity was non-significant or the random-effects model if significant heterogeneity was shown to exist^{34–36}.

Publication bias was investigated by visual inspections of funnel plots. Finally, sensitivity analyses for each class were performed to evaluate the influences of selected study and participant characteristics on study results.

Results

The literature search (Figure 1), which was to the best of my knowledge, exhaustive and comprehensive, yielded a total of 27 eligible studies after excluding unavailable articles, non-open-access reports, articles not in English, reviews and/or short reports, as well as those with unavailable or insufficient data. Of the 27 studies, respectively 20, 9, 4, 5, 10, 4 and 4 studies reported valid & usable data on the TFRC, AFRC, A-B RC, ATD, DAT, & ADT variables, which were incorporated into the meta-analysis. The characteristics of the 27 eligible studies^{37–63} are included in Table 2, while the excluded studies are elaborated in Table S1 within the Supplementary file S2.

Fingerprint patterns

The pooled effect sizes for all three fingerprint pattern datasets showed that significant heterogeneity was prominent (Figure 2–Figure 4). The OR datasets ranged from 0.24 to 2.27, 0.34 to 3.35, and 0.55 to 5.99 for the loops, whorls, and arches respectively. The pooled OR of the loops resulted in a significant effect size (OR = 0.76, 95% C.I. = 0.59–0.98, $z = 2.15$, $p = 0.03$), with decreased occurrence of loops among diabetic patients. In contrast, the pooled estimates for the whorls & arches resulted in non-significant effect sizes, with an OR of 1.30 (95% C.I. = 0.98–1.72, $z = 1.83$, $p = 0.07$) for whorls, and an OR of 1.19 (95% C.I. = 0.98–1.72, $z = 1.12$, $p = 0.26$) for the arches, indicating higher prevalence of both patterns among diabetic patients.

Total Finger Ridge Count (TFRC)

As is evident from the forest plot of TFRC effect sizes (Figure 5), the pooled effect sizes for the TFRC dataset were significantly heterogeneous ($I^2 = 85\%$, $p < .001$). The pooled estimate resulted in an insignificant effect size ($g = -0.03$, 95% C.I. = -0.29 – 0.22 , $p = 0.79$), with slightly lower TFRC among diabetic patients.

Absolute Finger Ridge Count (AFRC)

The forest plot of AFRC effect sizes (Figure 6) reveals no heterogeneity within the dataset, with the pooled estimate yielding a significant effect size ($g = 0.19$, 95% C.I. = -0.33 – 0.04 , $z = 2.58$, $p = 0.010$), with lower means prevalent among diabetic patients.

Total A-B Ridge Count (TABRC)

The pooled effect sizes for the palmar TABRC dataset (Figure 7) was significantly heterogeneous ($I^2 = 68\%$, $p = 0.01$), with the pooled estimate yielding slightly decreased but insignificant means among the diabetic subjects ($g = -0.02$, 95% C.I. = -0.25 – 0.21 , $z = 0.18$, $p = 0.85$).

ATD Angle

As is evident from the forest plot of TFRC effect sizes (Figure 8), pooled effect sizes for the palmar ATD angle dataset was significantly heterogeneous ($I^2 = 91\%$, $p < .001$). The pooled estimate resulted in a significant effect size ($g = 0.16$, 95% C.I. = -0.16 – 0.48 , $z = 0.99$, $p = 0.32$), with higher ATD angles among diabetics.

Figure 1. Flow diagram of search, evaluation, & exclusion/selection procedures.

TAD Angle

As depicted in [Figure 9](#), significant heterogeneity was observed for the DAT angle dataset ($I^2 = 72\%$, $p = 0.01$), with the pooled estimate showing an insignificant effect size ($g = -0.05$, 95% C.I. = -0.35 – 0.25 , $z = 0.33$, $p = 0.74$), with lower values expected among the group of diabetics.

ADT Angle

Similar to the DAT angle outcome, the ADT (TDA) angle dataset ([Figure 10](#)) was also significantly heterogeneous ($I^2 = 85\%$, $p < 0.001$), yet the pooled OR being insignificant. Herein, the pooled effect size indicated lower values of the ADT angle among diabetic patients ($g = -0.27$, 95% C.I. = -0.68 – 0.13 , $z = 1.32$, $p = 0.19$).

Analysis of publication bias via funnel plots and related tests are depicted in [Supplementary file S3](#), which indicate that it is unlikely that any significant publication bias occurred, but the necessity of considering several underlying factors from various angles is imperative, as discussed in the later sections. Sensitivity analysis for each dermatoglyphic variable & T2DM revealed that none of the studies influenced the results substantially.

Discussion

The current study is supportive of T2DM being a polygenic multifactorial disorder in which both genetic & environmental epigenetic insults cumulatively contribute to the disorder. The overall trend of

reduction in digital & palmar ridge counts, considered to be directly proportional to the growth rates during the 1st two trimesters of gestation, indicate abnormally delayed growth in diabetic cases than expected under normal conditions⁶⁴.

Similarly, the ATD angle is related to the axial triradius t position that migrates from the centre to the lower proximal portion of the palm during the early stages of gestation⁶⁵. Thus, distally deviating t positions imply prematurely halted t migrations or delayed developmental outcomes, resulting in increased ATD angles. The current analysis has observed increased (albeit insignificant) ATD increases among T2DM cases. Such findings evidence mild distortions of development during the early phases of gestational development.

The timing of epigenetic disturbances

One advantage of DG is that each variable is formed over a given gestational timeframe, thus enabling an estimation of the relative timing of developmental insults. This entails an assumption that the stressors specifically affecting an organ or system linked to the etiology of the disorder in question also had parallel bearings on the development of DG.

Regarding the fingerprint discrepancies, the current analysis has revealed that individuals with T2DM manifested significantly reduced loop patterns, counterbalanced by elevated whorl & arch frequencies. Evidences attest that pattern determination occurs

much earlier than the ridge proliferation, possibly influenced by the volar pad's shape, the embryonic epidermal axon development, or a combination of both^{18,66}. This asserts that patterns develop as early as weeks 6–11, thus indicating that the results of fingerprint discrepancies in this study evidence mid-to-late 1st trimester insults on the developing fetus.

Further, for comparison purposes, the arch & whorl patterns were pooled together regarding them as a common group of the “non-loops” & analyzed, which yielded heterogeneous but significant effect sizes [OR = 1.31; 95% C.I. = 1.02–1.68, $z = 2.15$, $p = 0.03$; $I^2 = 98\%$, $P < 0.01$], as depicted in the [Supplementary file S3](#).

Similarly, slightly reduced digital & palmar ridge counts were found to be characteristic of T2DM. Finger ridge counts are indicative of the rate of fetal growth during ridge development which occurs from the weeks 10.5 to 17, while palmar ridge counts (TABRC) are indicative of slightly later outcomes occurring over a wider timeframe and prone to reflect effects of non-shared environmental factors^{18,64,65}. Thus, the insignificant findings of TFRC & TABRC reductions, coupled with the significantly reduced AFRC (though the number of studies assessing this variable is low), are indicative of disruptive events occurring during gestation roughly between weeks 11 & 20, but of lesser effects as compared to the weeks prior to this.

Table 2. Characteristics of the studies included.

Author(s)	Year	Country of Study	Study Pop.	
			T2DM ^a	Healthy
Bala <i>et al.</i> ³⁷	2015	Gangtok, India	70	70
Burute <i>et al.</i> ³⁸	2013	Pune, India	101	100
Desai & Hadimani ³⁹	2013	Bijapur, India	100	100
Fuller ⁴⁰	1973	London	68	825
Gabriel & Babajide ⁴¹	2004	Nigeria	49	52
Karim & Saleem ⁴²	2014	Kurdistan, Iraq	50	50
Marera <i>et al.</i> ⁴³	2015	West Uganda	150	150
Mehta & Mehta ⁴⁴	2015	Hyderabad, India	100	100
Mittal & Lala ⁴⁵	2013	India	100	100
Nayak <i>et al.</i> ⁴⁶	2015	Maharashtra, India	50	50
Ojha & Gupta ⁴⁷	2014	Rajasthan, India	100	100
Pathan & Gosavi ⁴⁸	2011	Sholapur, India	100	100
Pathan & Hashmi ⁴⁹	2013	Sholapur, India	100	100
Rajanigandha <i>et al.</i> ⁵⁰	2006	India	112	142
Rakate & Zambare ⁵¹	2014	Maharashtra, India	350	350
Rakate & Zambare ⁵²	2013	Maharashtra, India	75	75
Ravindranath & Thomas ⁵³	1995	Bangalore, India	150	120
Sachdev ⁵⁴	2012	Rajasthan, India	100	150
Sengupta & Boruah ⁵⁵	1996	Assam, India	88	80
Sharma <i>et al.</i> ⁵⁶	2012	Rajasthan, India	50	50
Srivastava & Rajasekar ⁵⁷	2014	India	74	74
Sudagar <i>et al.</i> ⁵⁸	2014	Tamilnadu, India	150	150
Sumathi & Desai ⁵⁹	2007	Bijapur, India	100	100
Taiwo & Adebajo ⁶⁰	2012	Lagos, Nigeria	84	71
Trivedi <i>et al.</i> ⁶¹	2014	Gujarat, India	50	50
Udoaka & Lawyer-Egbe ⁶²	2002	Port Harcourt, Nigeria	90	90
Umana <i>et al.</i> ⁶³	2013	Zaria, Nigeria	101	126

Authorship, year of publication, country of origin of the sampled population, and sample sizes of the diabetic & healthy groups within the sampled population.

^aType-2 diabetes mellitus.

Figure 2. Forest plot of the association between loop fingerprint patterns & T2DM.

Figure 3. Forest plot of the association between whorl fingerprint patterns & T2DM.

Figure 4. Forest plot of the association between arch fingerprint patterns & T2DM.

Figure 5. Forest plot of the association between total finger ridge count (TFRC) & T2DM.

Figure 6. Forest plot of the association between absolute finger ridge count (AFRC) & T2DM.

Figure 7. Forest plot of the association between total A-B ridge count (TABRC) & T2DM.

Figure 8. Forest plot of the association between palmar angle ATD & T2DM.

Figure 9. Forest plot of the association between palmar angle DAT & T2DM.

Figure 10. Forest plot of the association between palmar angle ADT & T2DM.

Unlike disorders like schizophrenia, wherein epigenetic stressors have been attributed to prevail throughout the entirety of the gestational timeframe²⁹, the results of significant fingerprint pattern deviations and the insignificant TFRC, TABRC, and palmar angle discrepancies suggest that the insults must primarily be abundant during the early stages of gestation in T2DM. More specifically, events occurring during the mid-to-late 1st trimester have been underscored.

This stage of development witnesses key events of the endocrine pancreas development, whereby epigenetic insults could have maximum effects to result in structural & functional pancreatic defects. This period includes critical events in the prenatal development of the pancreas, including: development & fusion of ventral & dorsal primordial pancreatic buds (weeks 4–8), differentiation of the first insulin producing β -cells (weeks 7–9), as well as the clustering of endocrine cells & initiation of their subsequent association with the developing ducts of the pancreas (weeks 10–12)⁶⁷. Important tissues developing parallel with the pancreas (the Notochord & Mesenchyme), as well as key signaling pathways (Hedgehog & Notch) have also been shown to influence pancreatic organogenesis & underlying β -cell functioning^{67,68}.

Indications of an association between zygosity & fitness

Three lines of research suggest that fingerprint loops are associated with heterozygosity while arches & whorls are linked to homozygosity: (1) Population admixtures, which are known to increase genomic heterozygosity, have revealed significant loop frequency increases that are counterbalanced by non-loop (especially arch) pattern suppressions^{69,70}; (2) The occurrence of inbreeding or

endogamy, an opposite scenario to that of admixture & attributed to increased homozygosity, have been shown to decrease the loops while elevating the frequency of both non-loops^{71,72}; (3) The classical inheritance model of fingerprint patterns attributes two of the seven genes with cumulative bearings on multiple (all) fingers, both of which are dominant, favor the non-loop outcomes in the homozygous states. Further, loops have been shown to be an attribute of heterozygous conditions for most of the remaining five genes in this model¹⁶.

As advocated by the “heterozygote advantage” hypothesis⁷³, increased genomic homozygosity is associated with less viability, while an improved overall genetic fitness is attributed to increased heterozygosity. The decreased loop frequency together with the increased whorl & arch frequencies presumably represent increased homozygosity paralleled by a decreased heterozygosity in the T2DM, thus implying an overall decreased fitness in the former.

This can be interpreted via the concept of developmental homeostasis. An organism is regarded as developmentally stable based on how adequately it buffered against epigenetic disturbances during prenatal development, a capacity dependent on the interaction of genes with environmental conditions⁷⁴. With respect to the genotypic influences, homozygosity has been positively associated with decreased buffering capacity, while more genetically heterozygous organisms have been shown to be more resistant to developmental noise⁷⁵.

All in all, this zygosity-fitness-fingerprint correlation is in accordance with a string of reports on DG in T2DM & associated factors

such as obesity that incorporate variables that are more potent indicators of developmental deviations associated with reduced buffering capacities, including fluctuating asymmetry, dR45 (ridge-count difference between the 4th & 5th fingertips), and Md15 (mean RC both thumbs minus the mean RC of both little fingers)^{22–26}.

Supplementary evidence also originates from the previously discussed admixture changes. Heterozygosity underlying admixture was shown to be directly proportional to mean TFRC⁷⁰, from which it can be hypothesized that relative reductions in TFRC are indicative of increased homozygosity. The current analysis has shown that the T2DM group manifested reduced TFRC means which, though yielding non-significant pooled effect sizes, are in agreement with this hypothesis.

Limitations

Even with the exhaustive search protocols and stringent analysis methods characteristic of the current analysis, certain limitations of the study *per se*, as well as individual studies included in the analysis need be outlined:

- (1) Gender & ethnic discrepancies in DG are inherent features of normal populations^{76,77}. Since the individual reports included consisted of samples of mixed gender and/or ethnic affiliations, there lies a possibility that such polymorphisms masked some discrepancies possessing discriminating powers between the cases & controls that would otherwise have been evident.
- (2) Certain studies had underscored the presence of gender wise and/or right-left discrepancies among cases & controls for some of the dermatoglyphic variables. However, only the pooled data (for the right & left sides, as well as the males & females) was used in this analysis since the majority of the studies didn't provide such stratified data. This poses the possibility of neglecting markers of true discriminating powers for a specific gender or side.
- (3) It is known that T2DM is very heterogeneous, with distinct subtypes with parallel variations in underlying genetic determinants, such as maturity-onset diabetes of youth (MODY), latent adult-onset autoimmune diabetes, & diabetes secondary to rare genetic disorders shown to be part of the syndrome^{3,8,13}. Specific details, such as the ages-of-onset and other relevant specifications important in the determination of the relative homogeneity of the participants are virtually absent from all of the studies. This could be one possible explanation for the heterogeneity of the findings within a given variable type among the studies.
- (4) Similarly, the co-morbidity of disorders closely associated with DM, such as hypertension and cardiac disorders, were taken into consideration by a very limited number of studies only. This occurrence has been given little coverage,

even though such co-morbidity is expected to be a prevalent event⁷⁸, and the fact that each of these disorders are determined by distinct genetic & developmental outcomes parallel with the underlying deviations in the DG manifestations being distinct⁷⁹.

- (5) A number of reports were not included as they were not available as free (open-access) articles. A few were also noted to bear inconsistent or incomplete data, with corresponding authors unavailable or unwilling to aid in alleviating this obstacle.

Conclusions & recommendations

T2DM is orchestrated by the cumulative effects of a polygenic system with significant contributions from both pre- & postnatal environmental factors. Results of the current meta-analysis are indicative of epigenetic insults significantly linked to the 1st trimester, to a lesser extent on factors of the mid-second trimester, but least likely linked to those beyond the mid-second trimester in T2DM. Further, reduced heterozygosity possibly associated with a decreased buffering capacity to epigenetic stressors (developmental noise) during prenatal development has also been noted among the diabetic group. Based on these findings, the author recommends that future research aimed at expounding the prenatal origins of T2DM, as well as developing novel therapeutic methods, should focus on the early stages of endocrine pancreatic development.

Further, the Dutch Hunger Winter Families Cohort studies⁸⁰ have indicated the possibility of such a link between T2DM & prenatal environment, evident in the Md15 dermatoglyphic variable, to be associated with seasonal factors. An involvement of seasonal circumstances such as vitamin D or melatonin levels, as well as fetal toxicity caused by-products of surface water chlorine treatment has been hypothesized²⁶. It is recommended to undertake parallel studies from other global areas less prone to seasonality before ascertaining such hypotheses.

Finally, the author highlights on the necessity of advancing the currently existing knowledge on the molecular genetics of DG *per se*, as this would profoundly enhance their applicability as research tools to assess the genetic epidemiology of chronic disorders.

Competing interests

The author declares no competing interests.

Grant information

No grants/funding were involved in supporting this work.

Acknowledgements

We are highly grateful to all the academic & administrative staff of the University of Jigjiga for all their support & constructive comments forwarded during this analysis.

Supplementary materials

Supplementary file S1.

PRISMA Checklist

[Click here to access the data.](#)

Supplementary file S2.

Studies excluded from the meta-analysis, with the respective justifications

[Click here to access the data.](#)

Supplementary file S3.

Funnel-plots for testing publication bias

[Click here to access the data.](#)

References

- International Diabetes Federation. **IDF Diabetes Atlas (6th ed.)**. ISBN: 2-930229. 2013; 32–49.
[Reference Source](#)
- Rubino F: **Is type 2 diabetes an operable intestinal disease? A provocative yet reasonable hypothesis**. *Diabetes Care*. 2008; 31(Suppl 2): S290–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Zia A, Kiani AK, Bhatti A, *et al.*: **Genetic Susceptibility to Type 2 Diabetes and Implications for Therapy**. *J Diabetes Metab*. 2013; 4: 248–249.
[Publisher Full Text](#)
- Dayeh T, Volkov P, Salö S, *et al.*: **Genome-wide DNA methylation analysis of human pancreatic islets from type 2 diabetic and non-diabetic donors identifies candidate genes that influence insulin secretion**. *PLoS Genet*. 2014; 10(3): e1004160.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Frayling TM: **Genome-wide association studies provide new insights into type 2 diabetes aetiology**. *Nat Rev Genet*. 2007; 8(9): 657–662.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Sobngwi E, Mbanya JC, Unwin NC, *et al.*: **Exposure over the life course to an urban environment and its relation with obesity, diabetes, and hypertension in rural and urban Cameroon**. *Int J Epidemiol*. 2004; 33(4): 769–776.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Scott EM, Grant PJ: **Neel revisited: the adipocyte, seasonality and type 2 diabetes**. *Diabetologia*. 2006; 49(7): 1462–66.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Dancause KN, Veru F, Andersen RE, *et al.*: **Prenatal stress due to a natural disaster predicts insulin secretion in adolescence**. *Early Hum Dev*. 2013; 89(9): 773–6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Greene NH, Pedersen LH, Liu S, *et al.*: **Prenatal prescription corticosteroids and offspring diabetes: A national cohort study**. *Int J Epidemiol*. 2013; 42(1): 186–193.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Swaminathan K, Thangavel G: **Pesticides and human diabetes: a pilot project to explore a possible link**. *Practical Diabetes*. 2015; 32(3): 111–113.
[Publisher Full Text](#)
- Gerard J, van den Berg GJ, Pinger PR, *et al.*: **Instrumental variable estimation of the causal effect of hunger early in life on health later in life**. IFAU Institute for Evaluation of Labour Market & Education Policy, 2012; 6: 1–44.
[Publisher Full Text](#)
- Yajnik CS: **Commentary: Thrifty phenotype: 20 years later**. *Int J Epidemiol*. 2013; 42(5): 1227–1229.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Toperoff G, Aran D, Kark JD, *et al.*: **Genome-wide survey reveals predisposing diabetes type 2-related DNA methylation variations in human peripheral blood**. *Hum Mol Genet*. 2012; 21(2): 371–383.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Tobi EW, Slieker RC, Stein AD, *et al.*: **Early gestation as the critical time-window for changes in the prenatal environment to affect the adult human blood methylome**. *Int J Epidemiol*. 2015: 1–13.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Greenhill C: **Diabetes: DNA methylation affects T2DM risk**. *Nat Rev Endocrinol*. 2015.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Slatin HM, Katznelson MB, Bonn-Tamir B: **The inheritance of fingerprint patterns**. *Am J Hum Genet*. 1976; 28(3): 280–289.
[PubMed Abstract](#) | [Free Full Text](#)
- Medland S, Loesch DZ, Mdzewski B, *et al.*: **Linkage analysis of a model quantitative trait in humans: finger ridge count shows significant multivariate linkage to 5q14.1**. *PLoS Genet*. 2007; 3(9): 1736–1743.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Babler WJ: **Embryologic development of epidermal ridges and their configurations**. *Birth Defects Orig Artic Ser*. 1991; 27(2): 95–112.
[PubMed Abstract](#)
- Livshits G, Kobylansky E: **Fluctuating asymmetry as a possible measure of developmental homeostasis in humans**. *Hum Biol*. 1991; 63(4): 441–466.
[PubMed Abstract](#)
- Marn B, Fans L, Gutirrez B, *et al.*: **Dermatoglyphic Profile in 22q Deletion Syndrome**. *Am J Med Genet B Neuropsychiatr Genet*. 2004; 128B(1): 46–49.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Yohannes S, Alebie G, Assefa L: **Dermatoglyphics in diabetes: a prospective diagnostic aid & early preventive tool**. *Practical Diabetes*. 2015; 32(2): 1–3.
[Publisher Full Text](#)
- Kahn HS, Ravindranath R, Valdez R, *et al.*: **Fingerprint ridge-count difference between adjacent fingertips (dR45) predicts upper-body tissue distribution: evidence for early gestational programming**. *Int J Epidemiol*. 2001; 153(4): 338–344.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Ravindranath R, Joseph AM, Bosco SI, *et al.*: **Fluctuating asymmetry in Dermatoglyphics of non-insulin dependent diabetes mellitus in Bangalore-based population**. *Ind J of Hum Genet*. 2005; 11(3): 149–153.
[Publisher Full Text](#)
- Kahn HS, Graff M, Stein AD, *et al.*: **A fingerprint characteristic associated with the early prenatal environment**. *Am J Hum Biol*. 2008; 20(1): 59–65.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Kahn HS, Graff M, Stein AD, *et al.*: **A fingerprint marker from early gestation associated with diabetes in middle age: The Dutch Hunger Winter Families Study**. *Int J Epidemiol*. 2009; 38(1): 101–109.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Kahn HS, Stein AD, Lumey LH: **Prenatal environmental exposures that may influence -cell function or insulin sensitivity in middle age**. *J Dev Orig Health Dis*. 2010; 1(5): 300–309.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Alderson P, Green S, Higgins JPT: **Cochrane reviewers' handbook 4.2.2**. In: Cochrane Library, Issue 1. Chichester: Wiley. 2004.
[Reference Source](#)
- Moher D, Liberati A, Tetzlaff J, *et al.*: **Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement**. *PLoS Med*. 6(7): e1000097.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Golemb-Smith S, Walder DJ, Daly MP, *et al.*: **The presentation of dermatoglyphic abnormalities in schizophrenia: a meta-analytic review**. *Schizophr Res*. 2012; 142(1–3): 1–11.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Cummins H, Midlo C: **Finger prints, palms and soles : an introduction to dermatoglyphics**. Dover Publications, New York. 1961.
[Reference Source](#)
- Miller JR: **Dermatoglyphics**. *J Invest Dermatol*. 1973; 60(6): 435–442.
[PubMed Abstract](#) | [Publisher Full Text](#)

32. The Cochrane Collaboration. **Review Manager (RevMan) [Computer program].** Version 5.3. Copenhagen: The Nordic Cochrane Centre. 2014.
[Reference Source](#)
33. Higgins JP, Thompson SG, Deeks JJ, *et al.*: **Measuring inconsistency in meta-analyses.** *BMJ*. 2003; **327**(7414): 557–560.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
34. Mantel N, Haenszel W: **Statistical aspects of the analysis of data from the retrospective analysis of disease.** *J Natl Cancer Inst*. 1959; **22**(4): 719–748.
[PubMed Abstract](#)
35. DerSimonian R, Laird N: **Meta-analysis in clinical trials.** *Control Clin Trials*. 1986; **7**(3): 177–188.
[PubMed Abstract](#) | [Publisher Full Text](#)
36. Hunter JE, Schmidt FL: **Methods of meta-analysis: Correcting error and bias in research findings (2nd ed.).** Thousand Oaks, CA: Sage. 2004.
[Reference Source](#)
37. Bala A, Deswal A, Sarmah PC, *et al.*: **Palmar Dermatoglyphics patterns in diabetes mellitus and diabetic with hypertension patients in Gangtok region.** *Int J Adv Res*. 2015; **3**(4): 1117–1125.
[Reference Source](#)
38. Burute P, Kazi SN, Swamy V, *et al.*: **Role of Dermatoglyphic Fingertip Patterns in the prediction of Maturity Onset Diabetes Mellitus (Type II).** *IOSR-JDMS*. 2013; **8**(1): 1–5.
[Reference Source](#)
39. Desai SD, Hadimani GA: **Dermatoglyphics and Health.** *Anatomica Karnataka*. 2013; **7**(1): 1–9.
[Reference Source](#)
40. Fuller IC: **Dermatoglyphics: A Diagnostic Aid?** *J Med Genet*. 1973; **10**(2): 165–169.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
41. Gabriel SO, Babajide MO: **Dermatoglyphic patterns in diabetes mellitus in a south eastern Nigerian population.** *Afr J of Appl Zool & Environ Biol*. 2004; **6**: 6–10.
[Publisher Full Text](#)
42. Karim KJ, Saleem MA: **Dermatoglyphics Study of Finger Prints Pattern's Variations of a Group of Type II Diabetic Mellitus Patients in Erbil City.** *Zanco Journal of Pure and Applied Sciences*. 2014; **26**(4): 11–16.
[Reference Source](#)
43. Marera DO, Oyieko W, Agumba G: **Variation in Dermatoglyphic patterns among diabetics in Western Uganda population.** *African Journal of Science & Research*. 2015; **7**(3): 20–5.
[Reference Source](#)
44. Mehta AA, Mehta AA: **Study of fingerprint patterns in type II diabetes mellitus.** *Int J Anat Res*. 2015; **3**(2): 1046–1048.
[Publisher Full Text](#)
45. Mittal M, Lala BS: **Dermatoglyphics: An Economical Tool for Prediction of Diabetes Mellitus.** *Int J Med Health Sci*. 2013; **2**(3): 292–297.
[Reference Source](#)
46. Nayak V, Shrivastava U, Kumar S, *et al.*: **Dermatoglyphic study of diabetes mellitus Type 2 in Maharashtra population.** *Inter J Medical Sci Res Prac*. 2015; **2**(2): 66–69.
[Reference Source](#)
47. Ojha P, Gupta G: **Dermatoglyphic Study: A Comparison in Hands of Type 2 Diabetes Mellitus Patients and Normal Persons of Udaipur Region.** *JEMDS*. 2014; **3**(47): 1358–1368.
[Publisher Full Text](#)
48. Pathan FKJ, Gosavi AG: **Dermatoglyphics in Type II Diabetes Mellitus.** *MIMS Medical College, Latur's Journal of Medical Education & Research*. 2011; **1**(1): 6–8.
[Reference Source](#)
49. Pathan FKJ, Hashmi RN: **Variations of Dermatoglyphic Features in Non Insulin Dependent Diabetes Mellitus.** *IJRTST*. 2013; **8**(1): 16–19.
[Reference Source](#)
50. Rajnigandha V, Mangala P, Latha P, *et al.*: **Digito-Palmar Complex in Non-Insulin Dependent Diabetes Mellitus.** *Turk J Med Sci*. 2006; **36**(6): 353–355.
[Reference Source](#)
51. Rakate NS, Zambare BR: **Fingertip Patterns: A diagnostic tool to predict diabetes mellitus.** *Natl J Med Dent Res*. 2014; **2**(3): 49–53.
[Reference Source](#)
52. Rakate NS, Zambare BR: **Comparative study of the Dermatoglyphic patterns in type II diabetes mellitus patients with non diabetics.** *Int J Med Res Health Sci*. 2013; **2**(4): 955–959.
[Publisher Full Text](#)
53. Ravindranath R, Thomas IM: **Finger ridge count and finger print pattern in maturity onset diabetes mellitus.** *Indian J Med Sci*. 1995; **49**(7): 153–156.
[PubMed Abstract](#)
54. Sachdev B: **Biometric Screening Method for Predicting Type 2 Diabetes Mellitus among Selected Tribal Population of Rajasthan.** *Int J Cur Bio Med Sci*. 2012; **2**(1): 191–194.
55. Sengupta S, Boruah J: **Palmar dermatoglyphics in diabetes mellitus.** *The Bulletin of the Department of Anthropology, Dibrugarh University*. 1996; **24**: 73.
56. Sharma MK, Sharma H: **Dermatoglyphics: A Diagnostic Tool to Predict Diabetes.** *JCDR*. 2012; **6**(3): 327–332.
[Reference Source](#)
57. Srivastava S, Rajasekar SS: **Comparison of Digital and Palmar Dermatoglyphic Patterns in Diabetic and Non-Diabetic individuals.** *IOSR-JDMS*. 2014; **13**(7): 93–95.
[Reference Source](#)
58. Sudagar M, Radha K, Duraipandian K, *et al.*: **Study of palmar patterns in diabetic patients.** *Int J Adv Med*. 2014; **1**(2): 117–122.
[Publisher Full Text](#)
59. Sumathi S, Desai SD: **Study of Dermatoglyphics in Patients with Type II Diabetes Mellitus Essential Hypertension in the Age Group between 35-55 Years.** *Analytica Medica*. 2007; **10**(2): 22–28.
[Reference Source](#)
60. Taiwo IA, Adebajo OO: **Evaluation of association between digital dermatoglyphic traits and type-2 diabetes in Lagos, Nigeria.** *Nig Q J Hosp Med*. 2012; **22**(3): 191–199.
[PubMed Abstract](#)
61. Trivedi PN, Singel TC, Kukadiya UC, *et al.*: **Correlation of atd angle with Non-Insulin Dependent Diabetes Mellitus in Gujarati population.** *JRMDS*. 2014; **2**(2): 47–51.
[Publisher Full Text](#)
62. Udoaka AL, Lawyer-Egbe K: **Dermatoglyphic Patterns of Diabetic Mellitus Patients of Ijaw Origin in Port Harcourt, Nigeria.** *Niger J Health Biomed Sci*. 2009; **8**(2): 72–82.
[Publisher Full Text](#)
63. Umana UE, Bello R, Timbuk J, *et al.*: **Dermatoglyphic and Cheiloscopy Patterns among Diabetic Patients: A Study in Ahmadu Bello University Teaching Hospital Zaria, Nigeria.** *J Biol Life Sci*. 2013; **4**(2): 206–214.
[Publisher Full Text](#)
64. Cohen-Bendahan CC, van de Beek C, Berenbaum SA: **Prenatal sex hormone effects on child and adult sex-typed behavior: methods and findings.** *Neurosci Biobehav Rev*. 2005; **29**(2): 353–384.
[PubMed Abstract](#) | [Publisher Full Text](#)
65. David TJ: **Embryonic migration during the prenatal development of palm print patterns.** *Med Hypotheses*. 1981; **7**(5): 639–644.
[PubMed Abstract](#) | [Publisher Full Text](#)
66. Moore SJ, Munger BL: **The early ontogeny of the afferent nerves and papillary ridges in human digital glabrous skin.** *Brain Res Dev Brain Res*. 1989; **48**(1): 119–141.
[PubMed Abstract](#) | [Publisher Full Text](#)
67. Gittes GK: **Developmental biology of the pancreas: a comprehensive review.** *Dev Biol*. 2009; **326**(1): 4–35.
[PubMed Abstract](#) | [Publisher Full Text](#)
68. Gittes GK, Rutter WJ: **Onset of cell-specific gene expression in the developing mouse pancreas.** *Proc Natl Acad Sci U S A*. 1992; **89**(3): 1128–1132.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
69. Gutierrez SB, Lucenario JLS, Yebes MJT: **Dermatoglyphic studies among the Dumagat-Remontado tribal population of the Philippines.** *J Anthropol*. 2012; **1**–6.
[Publisher Full Text](#)
70. Cheng X, Li H, Gupta S, *et al.*: **Dermatoglyphic changes during the population admixture between Kam and Han Chinese.** *Homo*. 2009; **60**(2): 143–157.
[PubMed Abstract](#) | [Publisher Full Text](#)
71. Badaruddoza: **Effects of inbreeding on the finger print patterns.** *Anthropologist*. 2000; **2**(3): 193–195.
[Reference Source](#)
72. Țarcă A: **Dermatoglyphic indicators of illness risk for endogamous populations.** *J Prev Med*. 2002; **10**(1): 47–53.
[Reference Source](#)
73. Merrell DJ: **Ecological Genetics.** University of Minnesota Press, Minneapolis, 1981.
[Reference Source](#)
74. Kobylansky E, Bejerano M, Katznelson MB, *et al.*: **Relationship between genetic anomalies of different levels and deviations in dermatoglyphic traits-Dermatoglyphic sexual dimorphism in control healthy group of Israeli Jews.** *Studies in Historical Anthropology*. 2006; **4**: 61–121.
[Reference Source](#)
75. Zaidi ZF: **Body asymmetries: incidence, etiology and clinical implications.** *Aust J Basic Appl Sci*. 2011; **5**(9): 2157–2191.
[Reference Source](#)
76. Zhang HG, Chen YF, Ding M, *et al.*: **Dermatoglyphics from all Chinese ethnic groups reveal geographic patterning.** *PLoS One*. 2010; **5**(1): e8783.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
77. Yohannes S, Bekele E: **Ethiopian population dermatoglyphic study reveals linguistic stratification of diversity.** *PLoS One*. 2015; **10**(6): e0126897.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
78. Mannino DM, Thorn D, Swensen A, *et al.*: **Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD.** *Eur Respir J*. 2008; **32**(4): 962–969.
[PubMed Abstract](#) | [Publisher Full Text](#)
79. Eberchi DU, Gabriel OS, Peter OD: **A comparative study of the digital pattern, position of triradii, b-c and a-d palmar distances of diabetic subjects and essential hypertensive individuals in River State.** *Int J Adv Biotechnol Res*. 2012; **3**(2): 615–620.
[Reference Source](#)
80. Lumey LH, Stein AD, Kahn HS, *et al.*: **Cohort profile: the Dutch Hunger Winter families study.** *Int J Epidemiol*. 2007; **36**(6): 1196–204.
[PubMed Abstract](#) | [Publisher Full Text](#)

Open Peer Review

Current Peer Review Status:

Version 1

Reviewer Report 12 December 2016

<https://doi.org/10.5256/f1000research.7455.r17932>

© 2016 Otobo T. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Tarimobo Otobo

¹ Institute of Medical Sciences, University of Toronto, Toronto, ON, Canada

² Developmental and Stem Cell Biology, Peter Gilgan Centre for Research and Learning, Hospital for Sick Children, Toronto, ON, Canada

The title is properly framed and reflective of the study, with a precise summary. The study design and methodology meet the standards of meta-analysis. The use of dermatoglyphics as a surrogate marker of developmental instabilities is well documented in literature. However, the correlation is equivocal. But the author has been able to present a balanced and objective report within the limitations of the analyzed reports and this study.

The article has been reported with a reasonable depth of knowledge, providing the necessary information for replication.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 11 November 2015

<https://doi.org/10.5256/f1000research.7455.r10489>

© 2015 Wijerathne B. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Buddhika Wijerathne

Department of Forensic Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of

Sri Lanka, Anuradhapura, Sri Lanka

The main objective of this paper is to make a systematic review and meta-analysis of the association between dermatoglyphics and Type 2 Diabetes Mellitus. The systematic review was conducted in appropriate manner.

It is true that poor study designs, incorrect sample selections, overlooked confounding variables, made the reliability of many appraised studies questionable. The author has mentioned this in the limitation section. However, as this article is a systematic review and meta-analysis it is better to use a checklist like STROBE to assess the methodological quality of the observational studies. (<http://www.strobe-statement.org/>).

In results section it mentioned "Of the 27 studies, respectively 20, 9, 4, 5, 10, 4 and 4 studies reported valid & usable data on the"
What are these numbers? Are they references?

ATD angle is not a good variable in Dermatoglyphics studies for various reasons and therefore needs a little extension of discussion. In a recent review on hypertension and dermatoglyphics we have discussed this issue in detail. DOI: 10.1186/s40101-015-0065-3.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research