



UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
FACULTY OF HEALTH SCIENCES

SPECIFIC QUESTIONS TO BE ANSWERED BY EXAMINERS OF
THESES
SUBMITTED FOR DOCTOR OF PHILOSOPHY DEGREES

(This sheet should be detached and enclosed with the examiner's report)

PLEASE ANSWER "YES" OR "NO"

1.0 Does the thesis reveal a thorough acquaintance with the methods of research and the relevant literature, and a mastery of the necessary techniques? ..Yes.....

2.0 Does the thesis reveal that original work has been undertaken by the candidate? ...Yes.....

If your answer to this question is "yes", in what direction is the originality displayed?

The study is the first to examine Health Related quality of Life in a longitudinal fashion in a childhood brain tumour population and to compare the perspectives of both children and parents.

3.0 Does the thesis constitute a substantial contribution to the advancement of knowledge in the subject?Yes.....

4.0 Is the substance (though not necessarily the whole) of the thesis worthy of publication? ...Yes.....

5.0 Is the thesis satisfactory as regards literary style and presentation?Yes.....

6.0 Is the thesis adequate as the sole ground for the award of the degree?Yes

If **yes** - please specify what you recommend:

y

- Award of the degree, with no corrections?

- Award of the degree, subject to minor corrections to the satisfaction of the Head of Department

- Award of the degree, subject to substantial amendments, undertaken to the satisfaction of the Head of Department

X

7.0 If your answer to (6) is "no", would you recommend:

Substantial amendments, and re-examination?

Major revision, extension or elaboration and re-examination?

reject the research report outright?

Name of Candidate :Anthony Penn

Internal Examiner's report : A Penn PhD thesis (with responses in italics by Dr A. Penn)

The effect of childhood brain tumours on the child and the family

Quality of life is an elusive and difficult construct to define and measure and the current literature is fraught with controversies. I believe that this study in its prospective, longitudinal nature and its focus on the perspectives of both the children and the parents, adds a new dimension to the literature and has important implications for management. It is refreshing to see a focus on this topic which is not purely medical and given the increased incidence of childhood brain tumours, plus increasing survival rates, it is clear that the perspective should become more multidisciplinary and that long term outcomes must be a consideration for the clinician. The evidence accumulated in this study suggests importantly that the child's voice should be an important one in the team and that it is feasible and important to incorporate psychosocial measures into the test battery and management plan.

This is the first time I have had the opportunity to examine a thesis where the candidate has submitted publications for consideration. In this case I read the four submitted articles first. Though there is some overlap noted between these articles (in terms of content of Introduction and method sections for example) each one emphasizes a different aspect and there is no question that the work which has already been published and submitted to international peer review, is fully appropriate in originality, size and scope for a PhD.

Perhaps because this is a relatively new way of earning a PhD, I think some slight tweaks in format might be helpful in guiding the reader through the work (which I will suggest later). In general however I found this work to be original, comprehensive and well written and the comments which follow should be considered as constructive commentary with a goal to minor modification only.

The three background sections discuss brain tumours in children, quality of life and work that has been done on quality of life in children with primary intracranial tumours. The sections are logically organised, reflect wide reading and integration and an ability to evaluate critically methodological aspects. A thorough

evaluation has been done of prior research and this leads logically to the aims of the present study.

Two things stand out. The first is (as I have found in my own research) that an adequate definition of quality of life remains elusive and there is certainly room for improvement particularly for the paediatric population in specific area such as brain tumour. While the thesis considers this point very convincingly, it is a shame that the results of the thesis do not come any closer to suggesting a resolution or a refined definition for that area. I am sure that the writer has an idea but perhaps is too modest to say. Perhaps in the concluding section he could point us in the right direction or even suggest which tool might come closest to the tool of choice after analysis of the data.

I have made amendments to section 6.2. (Pg. 144 para 2 and 3) "Limitations of the Study" where I have commented on the use of the PedsQL and HUI2/3 in measuring HRQL. I have stated my preference for the PedsQL as a more acceptable measure of HRQL as the HUI is not subjective/preference based at the individual level, and does not have a social domain. I have also referred to the utility of using a BT-specific HRQL measure (Not available at the start of our study) for assessing HRQL in prospective studies such as the CLIC BT study, where HRQL is being assessed early after diagnosis.

The second is that the ubiquitous WHO model which frames so much of current QOL discourse has itself been modified fairly substantially and there needs to be an update in this thesis about that. The terminology of ICF has changed from impairment, disability and handicap for example to incorporate terms such as activity limitation and participation restriction- a shift which may well justify a closer examination and critique of some of the standard measure of Q of Life and motivate for a shift to include further participation and social dimensions in evaluation of quality of life.

I have updated the thesis to include modifications of the WHO model in chapter 1.6.2.1. (Pg. 17 and 18) I fully agree that HRQL scales should include social dimensions, and have voiced my opinion on the limitation of the HUI2/3 as a measure of HRQL due in part to its lack of a social scale (See comment above).

I have a feeling that a move to more qualitative methods (as the writer suggests in the final section) might encapsulate some of these critical dimensions. While on the one hand the use multiple measures strengthens the findings in the presence of a relatively small heterogeneous sample, one can't help feeling that the length and burden of these measures themselves may in some cases affect quality of life of the respondents negatively! After reading this study I am somewhat reassured that with a plethora of tools available at least some of them are picking up relevant factors ,but the search clearly remains for relevant and definitive tools and I have a sense that the writer is now in an informed position to suggest a viable one.

I agree with the above statement regarding tools used in measuring outcome. Too many tools were utilized in the study. However, the drop-out rate was extremely low for both patients and controls. I think this is most likely because almost all assessments took place in the family home, in a familiar environment for the family, but required a lot of travel and time on behalf of the assessors. This approach could not be replicated in the context of a large national or international clinical trial such as those most commonly employed in Paediatric Oncology. A more pragmatic approach is necessary which should include a measure of HRQL (PedsQL generic and brain tumour module) and perhaps an additional generic measure of behavioural function (SDQ, CBCL or similar questionnaire). There are unfortunately as yet no validated indirect measures of cognitive function so at present direct assessment is still necessary.

Method

The design of this study is excellent. Each aspect is carefully explained and the role of the writer made explicit. While this study was a part of a large scale study with numerous investigators the candidate's role in this study is clearly explained. We do indeed to see that this constitutes his own unaided work and that his contribution is original.

I feel that this aspect however should be explained earlier and what seems lacking is a brief introductory section/chapter which orients the reader to the thesis, describes the study and the prior publications and alerts the reader as

to what is to come.

The description of the CLIC Sargent Brain tumour study on p 90 would thus be better placed right at the beginning of the thesis. In this way the reader will better understand the focus of the background chapters and how this thesis emerged and how the candidate goes about claiming a niche. It would probably be helpful therefore for the research questions for this study to be stated clearly at the beginning. We need to see how and where the focus and to convince the reader of the individual and independent nature of the research.

As suggested by the examiner, I have moved the description of the CLIC Sargent Brain Tumour Study right to the front of the thesis, after the abstract (pg. x) , which should convince the reader of the individual and independent nature of the research I have amended the abstract to make the aims of the study more clear (pg vii, para 2.)

The fact that a normal control group was used as a comparison group is also an interesting feature of the design. The best friend's model seems very authentic. This is a particularly important aspect as I learn with interest that half of the sample was from an income deprived context.

To clarify, Nationally, using the IDACI scoring system, just under half of children (49%) live in families that are income deprived. I have removed this sentence to avoid ambiguity and have amended the definition of the IDACI in the Thesis (section 4.5.1 pg 96, para 2).

The potential impact of some of these contextual factors could possibly be further explored. Could for example educational level of the parents affect the utility of the tools in any way? Would cognitive and educational issues interact with these aspects and how? This seems particularly important given the mention made (p76/77) of how factors such as socioeconomic status influence outcomes aspects. The candidate also indicates that to date little work has been done and given the composition of this sample this would have been a useful further level of analysis. While certain of the demographic aspects are reported in the 4 studies, there is not much discussion on SES and I feel that

has potentially important implications. I wonder if SES status should not be put into the participant table on 113-this would enable the beginning of an analysis by such a factors. Ultimately I am not certain that we are looking for a tool which specifically excludes such factors from consideration as in a holistic model of rehabilitation there is no doubt that contextual factors will make a profound difference.

The IDACI rank scores have been included in the table on page 113 (Now page 111) of the initial submission as suggested. We analysed the brain tumour patients using direct correlation (Spearman's), according to quintile and finally based on whether they scored above or below the median score for our patients. For the purpose of the paper, on the advice of our statistician we used the median score as the discriminator, and this is reflected in the text of the Thesis and in the paper 2; "Family, demographic and illness related determinants of HRQL in children with brain tumours in the first year after diagnosis". Because there was no significant relationship between the IDACI and QOL/ HS, we did not include it in any further analysis in subsequent papers.

This has particularly important application for example in countries like South Africa with its huge linguistic and cultural diversity as well as a history of poor education and lack of access and agency. In selecting tools we need to know which works. Similarly measures of neuropsychological aspects (eg attention) are profoundly influenced by such factors. If these factors were not significant in this sample this finding should be explained given the nature of the group . The writer must have formulated some impressions and must have amassed a rich wealth of clinical and interview data to support the statistical findings.

As stated in the Limitations section of the study, we "aimed to perform a comprehensive assessment of the effects of brain tumour and its treatment on the child and family and to assess the interaction between tumour, treatment, family and child variables on QOL". While the student agrees that socio-economic factors are likely to be important in predicting outcomes such as HRQL/ HS, he had to be pragmatic when selecting independent variables. The "best friends" model was used in order to provide controls with similar socio-economic characteristics to study

subjects. With a limited number of subjects, and to minimize the chance of false positive results we choose a generic socio-economic measure that is well accepted and validated for the UK population (the IDACI score). We did this to ensure that there were no significant socio-economic differences between patients and controls which could potentially confound results, and to have a “generic” socio-economic independent variable in the study. Our approach has been similar for other independent variable such as the use of “radiotherapy” and “chemotherapy” as yes/no variables when the site, field and total dose of radiotherapy and the intensity of chemotherapeutic regimes may vary widely, dependent on tumour type and other disease risk factors (Please see pg. 143, para1).

The student has inserted potential reasons for the lack of significant correlation between socio-demographic factors and quality of life in the Conclusions section (pg. 141, para2). The student and supervisors feel that we have considered potential socio-economic moderators of QOL adequately, bearing in mind the aims and limitations of the study.

The findings of this study cannot be generalized to developing countries like South Africa because of the vast differences between them and developed countries like the UK. With many South African children with a brain tumour not receiving suitable treatment or even being properly diagnosed, survival rather than QOS is most often the primary aim. “Deprivation” and levels of education in the UK cannot be compared with that in South Africa and other developing countries. All but two of our subject/ control pairs were Caucasian in nature, and in all but one study pair English was the first language. Selection of an appropriate tool for measuring QOL in a developing country with multiple languages is well beyond the scope of this thesis and the student’s expertise!

The measures are well selected and the writer does show an awareness of limitations of some of these measures especially for younger age groups. Statistical measures are well justified and described and presented with a realistic understanding (both here and in the final section) of limitations imposed by numbers. I happen to believe that the longitudinal nature of this study more than compensates for that perceived shortcoming!

Integrating the four articles has been done in this thesis mainly through their clear summary and illustration in Section 5.1.3.

What I find lacking in places is some of the major findings described in the articles, being foregrounded in other appropriate places in the thesis. The abstract is a little over general and does not make reference to some specific and highly relevant findings (which can be found in the abstracts of the articles submitted)

This is a valid comment. With the abstract word count limit of 350 words we were unable to include all findings in it. We feel however that the most important findings are included with the exception of that raised by the examiner (See below).

For example the abstract makes no reference to the highly relevant finding that parents rated their children's HRQL lower than their child did.

The above has been added to the abstract.

Similarly the discussion section is rather brief and does not really explain the results or compare results with prior research (though this is done systematically in the articles), so there appears an imbalance between the comprehensive discussion in the introductory sections and the final section. Critical issues for example such as adaptive style are not explored further though they are intriguing. *The discussion section is brief in order to avoid repetition in the earlier sections, and in accordance with the student and supervisors' understanding of the "integrated format" for submission of the PhD.*

Highlights however are provided and limitations discussed. Implications are powerful and include many long term implication for the multidisciplinary rehabilitation team as well as the need for more work younger children and infants (see 131). *Overall* editorial care is good and tables and figures elucidating.

I look forward to the manuscripts in progress. I would like to suggest that a future publication takes two or three case studies from this sample and explores qualitatively, social, demographic and disease factors across time, linking it to parent and child responses on the measures and evaluating these measures in an ecologically illustrative way. This is the intriguing and fascinating world that the study has entered which can probably fruitfully be accessed in a more qualitative

way. The study has opened up endless possibilities for understanding the journey that children with brain tumours and their families have to cover.

Thank you for the excellent suggestions!

I have no hesitation in recommending the award of the degree subject to minor alterations to make the structure of this work as suggested above and some minor typos (listed below).

Structural alterations have been made as suggested.

I am grateful for the opportunity to read this work and congratulate the candidate and his supervisors.

Typos for correction

Note: I have corrected all typos and minor corrections suggested by all three examiners.

Not all abbreviations are listed in the abbreviations list and there must be a spelling out of the abbreviations when used for first time

Please list BT, PSC, MSC, QOS in list and also spell out QOS

at first use (p14) P27 4th line from bottom Replace their

with there

P37 replace practice with practice

P53 2nd line of table replace effected

with affected P10 14th line from bottom

on/On

P143 1st line second para: put apostrophes in patients' and controls'

Yours sincerely

A handwritten signature in blue ink, appearing to read 'A Penn', with a long horizontal stroke extending from the end.

Dr Anthony Penn
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