

LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



Harding, R; Selman, L; Simms, VM; Penfold, S; Agupio, G; Dinat, N; Downing, J; Gwyther, L; Ikin, B; Mashao, T; Mmoledi, K; Sebuyira, LM; Moll, T; Mwangi-Powell, F; Namisango, E; Powell, RA; Walkey, FH; Higginson, IJ; Siegert, RJ (2012) How to Analyze Palliative Care Outcome Data for Patients in Sub-Saharan Africa: An International, Multicenter, Factor Analytic Examination of the APCA African POS. *Journal of pain and symptom management*, 45 (4). pp. 746-52. ISSN 0885-3924 DOI: 10.1016/j.jpainsymman.2012.04.007

Downloaded from: <http://researchonline.lshtm.ac.uk/333672/>

DOI: [10.1016/j.jpainsymman.2012.04.007](https://doi.org/10.1016/j.jpainsymman.2012.04.007)

#### Usage Guidelines

Please refer to usage guidelines at <http://researchonline.lshtm.ac.uk/policies.html> or alternatively contact [researchonline@lshtm.ac.uk](mailto:researchonline@lshtm.ac.uk).

Available under license: <http://creativecommons.org/licenses/by-nc-nd/2.5/>

**How to analyse palliative care outcome data for patients in sub-Saharan Africa:  
an international multicentred factor analytic examination of the APCA African  
POS**

Richard Harding (*corresponding author*)

King's College London

Cicely Saunders Institute

Department of Palliative Care, Policy & Rehabilitation

Bessemer Road

London SE5 9PJ

UK

Email: [richard.harding@kcl.ac.uk](mailto:richard.harding@kcl.ac.uk)

Tel: +44(0)207485518 Fax: +44(0)2078485516

Lucy Selman

King's College London, Cicely Saunders Institute, UK.

Victoria Simms

King's College London, Cicely Saunders Institute, UK.

Suzanne Penfold

King's College London, Cicely Saunders Institute, UK.

Godfrey Agupio

Hospice Africa Uganda, Uganda.

Natalya Dinat

University of the Witwatersrand, South Africa.

Julia Downing

Formerly African Palliative Care Association, Uganda *and* King's College London,  
UK.

Liz Gwyther

Hospice Palliative Care Association of South Africa, South Africa.

Barbara Ikin

South Coast Hospice, South Africa.

Thandi Mashao

University of Cape Town, South Africa.

Keletso Mmoledi

University of the Witwatersrand, South Africa.

Lydia Mpanga Sebuyira

Infectious Disease Institute, Uganda.

Tony Moll

Philanjalo Hospice, South Africa.

Faith Mwangi-Powell

African Palliative Care Association, Uganda.

Eve Namisango

African Palliative Care Association, Uganda.

Richard A Powell

African Palliative Care Association, Uganda.

Frank Walkey

School of Psychology, Victoria University of Wellington, New Zealand.

Irene J Higginson

King's College London, Cicely Saunders Institute, UK.

Richard Siegert

King's College London, Cicely Saunders Institute, UK.

**Tables:** 3

**Figures:** 0

**References:** 20

**Word Count:** 2355

## **Abstract**

### *Background*

The incidence of life-limiting progressive disease in sub-Saharan African presents a significant clinical and public health challenge. The ability to easily measure patient outcomes is essential to improving care.

### *Objectives*

The present study aims to determine which specific factors (if any) underpin the APCA Africa POS in order to assist the analysis of data in routine clinical care and audit.

### *Methods*

Using self-reported data collected from HIV patients in Eastern and Southern Africa, firstly an exploratory factor analysis was undertaken on n=1337 patients, and subsequently a confirmatory analysis on two samples from separate datasets n=445.

### *Results*

Using exploratory factor analysis initially, both two and three factor solutions were examined and found to meet criteria for simple structure and be readily interpretable. Then using confirmatory factor analysis on two separate samples, the three factor solution demonstrated better fit, with GFI values above 0.95 and NFI values close to 0.90. The resulting three factors were 1. Physical and psychological well-being. 2. Interpersonal well-being. 3. Existential well-being.

### *Conclusion*

This analysis presents an important new opportunity in the analysis of outcome data for patients with progressive disease. It has advantages over both the total scoring of multidimensional scaling (which masks differences between domains) and of item scoring (which requires repeated analyses). The three factors map well onto the underlying concept and clinical goals of palliative care, and will enable audit of facility care.

**Running title:** Factor analysis of African palliative outcome data

**Keywords:** Palliative, progressive, HIV, cancer, factor analysis, Africa, outcome measure.

## Background

For patients with life-limiting progressive disease, palliative care is necessary throughout the disease trajectory, due to the multidimensional (physical, psychological, social and spiritual) problems that are experienced (1-6). Therefore, palliative care is advocated by the World Health Organisation for the 22.4 million people in sub-Saharan Africa who live with HIV infection, the 1.4 million of those who die annually (7), and the 542,000 patients who die of cancer annually in sub-Saharan Africa and their family members (8).

Despite the epidemiology of progressive disease in Africa, and the need to measure and improve outcomes for infected persons and their families, there has been a dearth of evidence (9) of outcomes and effectiveness. The ability to measure and improve care is essential in responding to the need for effective palliative care, and African patients also deserve measurable care that can be demonstrated to improve the outcomes that matter to them and their families. In order to enable clinicians and researchers to measure outcomes in patients with progressive conditions in Africa, the APCA African POS was developed in 8 sub-Saharan African countries (10) and validated at 5 sites (11). The African Palliative Care Association African Palliative Outcome Scale (APCA African POS) uses the approach of the original POS, which is a widely used tool that has been validated and applied in a number of regions around the world (12).

The APCA African POS consists of 10 items, seven of which are oriented to the patient (and are the subject of the factor analysis presented here) and three to the family, and has good psychometric properties. Each item is scored from 0-5, with

**Commented [I1]:** Please update this reference to:  
<http://www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-031574.pdf>

reversed scoring for some items to indicate worst possible outcome. Each of the items can be scored and considered separately, and they can also be summed to yield a total score. It is currently the only multidimensional tool that has been fully validated in African palliative care populations. It has been translated into local languages in East and Southern Africa as well as an English version.

For those who use tools to measure patient outcomes, factor analysis can reduce the number of variables to a number that reflect the underlying areas of interest being measured. Therefore, in addition to analysing a tool using a summative (or total score), or analysing by all individual items, it is possible to measure a small number of variables (or factors) that describe outcomes in a number of fields that can be appraised and clinically responded to. A recent factor analytic study of the 10 item POS with UK patients reported two factors underpinning: one reflecting psychological status and the other quality of care (13).

The present study aims to determine which specific factors (if any) underpin the APCA Africa POS in order to assist the analysis of data in routine clinical care and audit.

## **Methods**

### *Design*

This study was a secondary analysis of cross-sectional APCA African POS data from a sample of patients with incurable progressive illness at 17 HIV or palliative care facilities in three sub-Saharan countries (Kenya, Uganda and South Africa). Data were collected as part of two larger studies: the HIV care and support Public Health Evaluation (14) and the ENCOMPASS validation study of the APCA African POS (11). These are described separately below.

### *Setting*

**Public Health Evaluation:** This study was conducted in public health HIV facilities in Kenya and Uganda in 2009-2010. One hundred adult outpatients with confirmed HIV diagnosis were consecutively recruited at each of 12 of the largest PEPFAR-funded sites (total n=1337 patients) from a stratified random sample of facilities. Stratification was by patient population size, and all 12 sites provided outpatient HIV care and support. The exclusion criteria were facilities that were paediatric-only or inaccessible (e.g. insecure, no road access). Data included in the analysis were from the baseline data of this longitudinal study.

**ENCOMPASS study:** This study was conducted in three non-profit palliative care services and one state service in South Africa, and one voluntary sector hospice service in Uganda during 2008-2009. Criteria for selecting the five participating sites were: established palliative care services able to support research and fulfil recruitment criteria for the study, and representing a range of service types (home-based care and inpatient units) and locations (rural, urban township and urban), in order to enhance the generalisability of findings (15). All services aimed to offer holistic palliative care in line with the WHO definition (16), provided by multi-professional teams. Two cross-sectional surveys using the POS were conducted on



two separate samples (sample 1 n=215; sample 2 n=230) and both datasets were analysed in this study.

#### *Data collection and management*

Public Health Evaluation: Following informed consent, research staff took demographic details (age, gender, number of dependents, ECOG functional status (17) and read aloud the APCA African POS, and respondents gave verbal responses which the researcher recorded. All data were double entered into EpiData, cleaned and checked. Any discrepancies during data checks were reconciled with reference to the original paper questionnaire. All participants were paid \$5 expenses for participation to cover the cost of transport, sustenance and opportunity cost of attendance.

ENCOMPASS: Following informed consent, research staff took demographic details (age, gender, number of dependents, ECOG functional status) and read aloud the APCA African POS, and respondents gave verbal responses which the researcher recorded. Data were entered into Excel spreadsheets and checked for errors; discrepancies during data checks were reconciled with reference to the original paper questionnaire.

#### *Ethics*

Ethical approval for the Public Health Evaluation was granted by King's College London (CREC/06/07-140), the Ugandan National Council for Science and Technology (SS 1964) and the Kenyan Medical Research Institute (KEMRI/RES/7/3/1). Ethical approval for the ENCOMPASS study was granted by the Universities of Cape Town (128/2006), KwaZulu Natal (E025/06) and Witwatersrand (M060366), the Ugandan National Council for Science and Technology (HS143),

Hospice Africa Uganda, and the Hospice Palliative Care Association of South Africa (001/06).

### *Analysis*

The data were imported into PASW Statistics-18 for exploratory factor analyses and AMOS-18 for confirmatory analyses.

Analysis 1: In analysis 1 we used principal component analysis (PCA) and Varimax rotation to explore the factor structure of the APCA African POS as these typically result in relatively clear, interpretable solutions (18, 19). The exploratory factor analysis (EFA) examined two and three-factor rotated solutions using the sample of 1,337 participants from the Public Health Evaluation.

Analysis 2: To compare the robustness of the two and three factor solutions we examined both solutions using confirmatory factor analysis (CFA). The advantage of CFA over EFA is that it does not rely solely upon a judgement based on visual inspection of the rotated factor loadings as in EFA, but produces a goodness-of-fit test that quantifies how well the data actually fit the hypothesised model. We obtained four indices of goodness of fit. These indices and cut-off values are recommended by Ullman who also advises against relying upon any one single index(20). The first was chi-square. Here we sought a low, non-significant value, which would indicate a close fit between the data and the model. However, as this index can be misleading with large samples, Ullman has proposed that as a rule-of-thumb a chi-square to degrees of freedom ratio (chi-square/df) of less than 2.00 may be deemed to reflect a good fit to the model (20). This ratio was therefore used as our second index. For our third index, we used the goodness of fit index (GFI) where we sought a high value, approaching 1.00 and preferably > 0.95, to indicate a good fit to the model. The fourth fit index we used was the Normative Fit Index (NFI) where values greater than 0.90 indicate a good fitting model (20). Finally, for our fifth

index, we used the root mean square of approximation (RMSEA), which may be thought of as a measure of badness of fit, in which we therefore sought a very low value, approaching 0.00 and preferably  $< 0.06$  to indicate a good fit.

The CFA was performed on two separate datasets from the ENCOMPASS study ( $n=215$  and  $n=230$ ). A very small number of missing data points ( $n=5$ ) in the second ENCOMPASS data set were replaced with a '2' (i.e. the mid-point on the response scale). Using the mid-point of the scale has a neutral effect on any correlations employed in the subsequent factor analyses. It thus allowed us to retain and use the full data set while not affecting any results.

## Results

### *Sample characteristics*

Public Health Evaluation sample: Of the 1337 participants, 696 were from Kenya and 641 from Uganda. For the entire sample, the mean age was 34.8 (SD 9.0), 68.3% were female, and they had a median of 4 dependents. Their functional status ECOG score (17) was as follows: fully active n=803 (60.1%); restricted n=408 (30.5%); ambulatory n=102 (7.6%); limited self care n=21 (1.6%); completely disabled n=2 (0.2%) (missing n=1).

ENCOMPASS Sample 1: Of the 215 patients, 40 were from Uganda and 175 from South Africa. The mean age across the sample was 37.3 (SD 10.4); 66.0% were female; the mean number of dependents was 2.9 (SD 2.0, range 1-12). 11.2% of patients also had a cancer diagnosis. ECOG scores were: fully active n=23 (10.7%), restricted n=47 (21.9%), ambulatory n=51 (23.7%), limited self care n=72 (33.5%), completely disabled n=22 (10.2%).

ENCOMPASS Sample 2: Of the 230 patients, 46 were from Uganda and 184 from South Africa. The mean age across the sample was 36.7 (SD 9.5); 70.9% were female; the mean number of dependents was 2.4 (SD 1.9, range 0-12). 15.2% also had a cancer diagnosis. ECOG scores were: fully active n=17 (7.4%), restricted n=55 (23.98%), ambulatory n=68 (29.6%), limited self care n=72 (31.3%), completely disabled n=18 (7.8%).

### *Analysis 1*

The result of the PCA for the Public Health Evaluation sample (n=1337) is presented in Table 1. Two components were identified with an eigenvalue greater than one, and together these two components accounted for 49% of the total variance. The scree

plot also indicated a two factor solution. Inspection of Table 1 reveals two components of which one is primarily concerned with internal physical symptoms and psychological well-being, and the other with the patient's external interactions and relationship with their family. While these results seemed to indicate a reasonably good two factor solution, we examined both two and three factor rotated solutions to reduce the potential for 'under-factoring'.

The results of the two and three-factor rotated solutions are presented in Table 2. The two factor rotated solution is virtually identical to the solution from the PCA, and hence strongly suggests two orthogonal or uncorrelated factors. The first factor comprising items 1, 2, 3 and 6 is primarily concerned with the individual burden of disease in terms of physical wellbeing (pain, symptoms) and existential wellbeing (worry, peace) and the second factor with an interpersonal dimension. The three factor solution, which accounted for 63% of the total variance, also seemed to provide a readily interpretable solution suggesting three factors – with Factor 1 reflecting symptoms including physical and psychological symptoms, Factor 2 interpersonal, and Factor 3 an existential dimension. As both the two and three factor solutions met criteria for simple structure and seemed interpretable we compared both models on two independent data sets using CFA.

#### *Analysis 2*

We tested a two factor model in which items 1, 2, 3 and 6 comprise one factor and items 7 and 4 a second factor and the two factors were correlated, and a three factor model where items 1, 2 and 3 comprise one factor, items 4 and 7 a second and items 5 and 6 a third factor. Both models were tested on both samples. The results for the two and three factor models tested in Sample 1 and Sample 2 are displayed in Table 3. Inspection of Table 3 demonstrates that the three factor model showed much better fit across both of the samples. Indeed the two factor model shows quite poor fit

as reflected in NFI values well below 0.90, and RMSEA values both above 0.10. In contrast the three factor model has quite good fit, as reflected in both GFI values above 0.95, and both NFI values close to 0.90.

## Discussion

In the present study we examined the stability of two and three factor solutions across 1337 patients with HIV infection. We observed a reasonably clear three-factor solution that comprised the following factors: Factor 1. Physical and psychological wellbeing, Factor 2. Interpersonal wellbeing and Factor 3. Existential wellbeing. These three factors were confirmed in two independent samples of 215 and 230 patients receiving palliative care. These results provide evidence of the major dimensions that underpin the APCA African POS items, and hence support the construct validity of the measure. The APCA African POS is currently being used as an outcome tool for research to evaluate palliative care in East and Southern Africa, as a primary outcome in clinical trials, and as a routine clinical assessment tool. There are a number of study limitations, and the results need to be considered in this context. While the three-factor solution demonstrated reasonably good fit and makes intuitive clinical sense, it was not a perfect fit. Only one goodness-of-fit index (the GFI) indicated excellent fit with three (Chi Square/df, NFI and RMSEA) only falling close to the cut-off for very good fit. Thus the three factor model was clearly superior to the two factor model but showed adequate rather than excellent fit. This might be because we completed the exploratory factor analysis on a large sample from Kenya and Uganda and ran the confirmatory analyses on two smaller samples from South Africa and Uganda – and there were differences in the clinical characteristics of the respective samples. For example, the samples from the Encompass study were more functionally restricted than in the Public Health Evaluation study. Hence clinical differences in the exploratory and confirmatory factor analysis samples might explain the less than perfect fit achieved. Certainly it would be desirable to replicate these results with an independent sample. Interestingly the three factor structure reported here (psychological well-being, interpersonal well-being and existential well-being) is somewhat different from the

two factors (psychological well-being and quality of care). This might reflect cultural differences with family and spirituality being highly important for most African participants (2) or it could reflect differences in the clinical composition of the African and UK samples. It is important to note here that the UK version of the POS has ten items compared with the seven item APCA African POS – and this might also account for some of the differences in factor structures reported.

On an individual patient basis when using the tool to assess and inform care planning, we recommend that clinicians consider the total score for all seven items and check all seven items individually for elevated scores. However, we propose that the three factor solution provides an appropriate conceptual summary of the important areas of clinical concern here, namely: physical and psychological, interpersonal, and existential well-being. The advantage of the provision of dimensions (i.e. factors) over total scoring of a multidimensional tool is that a total score may mask change that is not routinely of the same direction and magnitude across items. The ability to score factors offers a useful analytic approach that allows a reduced number of variables while still enabling clinicians and researchers to report patient outcomes according to the underlying domains that constitute multidimensional palliative care. Therefore, the use of these factors offers a reduced scoring system to three clear and stable factors, and we recommend that clinicians use these at audit level to enable a simple approach to measuring and improving care at the facility level. For researchers, the provision of these domains enable the analysis of three subscales that map clearly onto the goals of palliative care, and offer the opportunity to conduct fewer analyses than using individual items while offering a more detailed analysis than using a total score. This analysis therefore provides a new opportunity to measure and improve care for patients with progressive, life-limiting illness in sub-Saharan Africa.

#### **Disclosures and Acknowledgements**



We are grateful to the funders who supported the data collection that contributed to this analysis: the BIG Lottery Fund UK under grant number IG/1/010141040, and the United States Agency for International Development for funding this study under sub-agreement GPO-A-00-03-00003-00, made under the authority provided to the University of North Carolina. The funder was not involved in the conduct of the study or development of this submission.

The authors declare that they have no conflicts of interest.

**Table 1: Principal Component Analysis of the APCA African POS (n=1337)**

ITEM	Component 1	Component 2
Q3 Worried about illness	.71	
Q1 Pain	.71	
Q6 Felt at peace	.69	
Q2 Other symptoms	.64	
Q7 Help and advice/family		.74
Q4 Share feelings/family		.67
Q5 Felt life worthwhile		.41

\* All loadings rounded to two decimal places and loadings < .35 hidden for clarity.

**Table 2: Two and Three Factor Varimax Rotated Solutions for the APCA African POS (n=1337)**

Item	Factor1	Factor 2	
Q1 Pain	.71		
Q3 Worried about illness	.71		
Q6 Felt at peace	.68		
Q2 Other symptoms	.64		
Q7 Help and advice/family		.74	
Q4 Share feelings/family	-.35	.66	
Q5 Felt life worthwhile		.42	
	Factor1	Factor 2	Factor 3
Q1 Pain	.75		
Q2 Other symptoms	.73		
Q3 Worried about illness	.67		
Q7 Help & advice/family		.82	
Q4 Share feelings/family		.74	
Q5 Felt life worthwhile			.90
Q6 Felt at peace	.51		.59

\* All loadings rounded to two decimal places and loadings < .35 hidden for clarity.

**Table 3. Results of the Two and Three Factor Confirmatory Factor Analyses for Two Samples**

<b>Index of Fit to the Model</b>	<b>Two Factors</b>	<b>Three Factors</b>	<b>Two Factors</b>	<b>Three Factors</b>
<b>Sample</b>	ENCOMPASS Sample 1 N=230	ENCOMPASS Sample 1 N=230	ENCOMPASS Sample 2 N=215	ENCOMPASS Sample 2 N=215
<b>Chi-square</b>	94.82	35.47	55.60	24.50
<b>Df</b>	13	11	13	11
<b>p =</b>	0.00	0.00	0.00	0.01
<b>Chi-square/df</b>	7.29	3.22	4.28	2.22
<b>GFI</b>	0.89	0.96	0.93	0.97
<b>NFI</b>	0.62	0.86	0.68	0.86
<b>RMSEA</b>	0.17	0.10	0.12	0.08

## Reference List

1. Sepulveda C, Habiyambere V, Amandua J, Borok M, Kikule E, Mudanga B, et al. Quality care at the end of life in Africa. *BMJ*. 2003;327(7408):209-13.
2. Selman LE, Higginson IJ, Agupio G, Dinat N, Downing J, Gwyther L, et al. Quality of life among patients receiving palliative care in South Africa and Uganda: a multi-centred study. *Health QualLife Outcomes*. [1477-7525-9-21 pii ;10.1186/1477-7525-9-21 doi]. 2011;9(1):21.
3. Harding R, Selman L, Agupio G, Dinat N, Downing J, Gwyther L, et al. The prevalence and burden of symptoms amongst cancer patients attending palliative care in two African countries. *Eur J Cancer*. 2011 Jan;47(1):51-6.
4. Wakeham K, Harding R, Bamukama-Namakoola D, Levin J, Kissa J, Parkes-Ratanshi R, et al. Symptom burden in HIV-infected adults at time of HIV diagnosis in rural Uganda. *J PalliatMed*. [10.1089/jpm.2009.0259 doi]. 2010;13(4):375-80.
5. Peltzer K, Phaswana-Mafuya N. The symptom experience of people living with HIV and AIDS in the Eastern Cape, South Africa. *BMC Health ServRes*. [1472-6963-8-271 pii ;10.1186/1472-6963-8-271 doi]. 2008;8:271.
6. Kikule E. A good death in Uganda: survey of needs for palliative care for terminally ill people in urban areas. *British Medical Journal*. 2003;327(7408):192-4.
7. UNAIDS. AIDS Epidemic Update 20092009 Contract No.: [http://data.unaids.org/pub/Report/2009/JC1700\\_Epi\\_Update\\_2009\\_en](http://data.unaids.org/pub/Report/2009/JC1700_Epi_Update_2009_en).
8. American Cancer S. Global cancer: facts and figures 2007. US2007.
9. Harding R, Higginson IJ. Palliative care in sub-Saharan Africa. *The Lancet*. 2005;365(9475):1971-7.
10. Powell RA, Downing J, Harding R, Mwangi-Powell F, Connor S. Development of the APCA African Palliative Outcome Scale. *J Pain Symp Manage*. 2007;33(2):229-32.
11. Harding R, Selman L, Agupio G, Dinat N, Downing J, Gwyther L, et al. Validation of a core outcome measure for palliative care in Africa: the APCA African Palliative Outcome Scale. *Health QualLife Outcomes*. [1477-7525-8-10 pii ;10.1186/1477-7525-8-10 doi]. 2010;8:10.
12. Hearn J, Higginson IJ. Development and validation of a core outcome measure for palliative care: the palliative care outcome scale. *Palliative Care Core Audit Project Advisory Group. Qual Health Care*. 1999 Dec;8(4):219-27.
13. Siegert RJ, Gao W, Walkey FH, Higginson IJ. Psychological well-being and quality of care: a factor-analytic examination of the palliative care outcome scale. *J Pain Symptom Manage*. 2010 Jul;40(1):67-74.
14. Harding R, Simms V, Penfold S, McCrone P, Moreland S, Downing J, et al. Multi-centred mixed-methods PEPFAR HIV care & support public health evaluation: study protocol. *BMC Public Health*. [1471-2458-10-584 pii ;10.1186/1471-2458-10-584 doi]. 2010;10:584.
15. George LK. Research design in end-of-life research: state of science. *The Gerontologist*. 2002;42(S3):86-98.
16. Who. Definition of palliative care. 2011; Available from: <http://www.who.int/cancer/palliative/definition/en/>.
17. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. *American Journal of Clinical Oncology*. 1982;5:649-55.

18. Pett M, Lackley N, Sullivan J. Making Sense of Factor Analysis: The Use of Factor Analysis for Instrument Development in Health Care Research. . Thousand Oaks: Sage Publications; 2003.
19. Thompson B. Exploratory and Confirmatory Factor Analysis: Understanding Concepts and Applications. Washington DC: American Psychological Association; 2004.
20. Ullman J. Structural equation modelling. In: Tabachnick B, Fidel LE, editors. Using multivariate statistics. 4th edition ed. Needham Heights: Allyn & Bacon; 2001. p. 653–771.