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Impact of pharmaceutical care interventions on the CD4+ lymphocytes counts (therapeutic outcome) of patients on antiretroviral drugs

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Abstract

CD4 count and viral load determine the progression of HIV infection. HIV actively infects and destroys CD4 cells. High viral load results in higher transmission risk and is also a sign of more severe disease. Measurements of CD4 counts can be used as an indirect means of estimating HIV viral load and as such determine disease progression and/or therapeutic outcome of antiretroviral therapy. Pharmaceutical care (PC) has been shown to improve the outcome of drug therapy in many disease conditions. HIV/AIDS is one of the disease conditions that are fraught with many problems that can benefit from this new emphasis of pharmacy practice also known as 'pharmacists care'. This study is designed to evaluate the impact of pharmaceutical care activities on the CD4 cell counts of HIV/AIDS patients receiving antiretroviral drugs. The components of the American society of health-system pharmacists (ASHP) guidelines on 'standardized method for pharmaceutical care' was used as a data collection instrument to evaluate, document and intervene and re-evaluate the antiretroviral therapy of about one thousand four hundred and seventy three (1,473) patients. The results showed that that 55.2% of the patients recorded significant increases in their CD4 cells count, 14.1% of them maintained their pre - intervention CD4 cells count while 10.3% of them recorded decreases in their CD4 cell count. However, in 20.4% of the patients the CD4 cell counts could not be determined. The study showed that pharmacists' interventions in antiretroviral drug therapy through Pharmaceutical care can significantly improve the CD4 cells counts of patients receiving antiretroviral drugs hence therapeutic outcome of antiretroviral drug therapy.

Keywords: Pharmaceutical care, HIV/AIDS, CD4 cell Counts, Pharmacist Interventions, Hospital Pharmacy

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1. Introduction

Pharmaceutical care (PC) has been defined as the responsible provision of drug therapy for the purpose of achieving definite outcomes that improves or maintains a patient's quality of life (Hepler & Strand, 1990) as modified by (FIP, 1998). The concept of pharmaceutical care is about pharmacists taking more responsibility for the outcome of drug therapy. It affects the way the pharmacist thinks and acts in relation to patients and has become a dominant aspiration of pharmacy practice worldwide in the past decade and aims to improve the following patient outcomes - clinical outcome, humanistic outcome and economic outcome (Oparah, 2004). HIV/AIDS on the other hand is possibly the biggest challenge facing the healthcare system today. It is a condition that occurs when the HIV organism (a retrovirus) weakens the human immune system. Infection with the virus is a dynamic process characterized by vigorous viral replication, CD4 lymphocyte depletion and profound immune deficiency.

The concept and philosophy of pharmaceutical care has been adopted and implemented in many developed countries for many years now. It has achieved great successes in the care of patients in the US, UK and other developed countries of the world as patients in these places now get better care from Pharmacists who alongside the patients and healthcare managers are delighted about the initiative (Erah & Nwazuoke, 2002).

Antiretroviral drug therapy (ART) has faced serious challenges despite much progress and many patients still do not benefit from it due to viral resistance, adverse effects of chronic therapy , lack of adherence to complex regimens, unavailability of current agents in the developing countries (where the pandemic has its greatest impact). The consequences of these have been devastating to the patients, healthcare system and many countries. Controlling the disease will involve ensuring that the patients receiving treatment get the maximum benefits of drug therapy. Thus the management of HIV/AIDS infection is one situation that has brought to the front burner the issue of establishing pharmaceutical care in healthcare systems [world over] (Obodozie, 2006). Hence the role of the Pharmacist in healthcare through the concept of pharmaceutical care has become imperative in the global struggle to save humanity from extinction due to HIV/AIDS.

CD4 is molecule (receptor) on the surfaces of cells of the immune system (including monocytes, macrophages, glial cells and T-cells lymphocytes also called CD4 cells or helper T-cells or T-cells) onto which the HIV surface glycoprotein binds. CD4 count and viral load determine the progression of HIV infection. HIV actively infects and destroys key cells of the immune system specifically CD-4 cells/ lymphocytes which reside mainly in the lymph nodes as well as other tissues of the body. These CD-4 cells are responsible for a

number of functions including regulation of host's cell mediated immunity. Viral load is the amount of HIV in the blood and is measured by the HIV ribonucleic acid polymerase chain reaction test (HIV - RNA PCR). The viral load is very high immediately after primary HIV infection but starts decreasing with development of cellular immune response to the infection. Therefore it falls when the body develops antibodies and rises again after a period as the CD4 count drops. High viral load results in higher transmission risk and is also a sign of more severe disease.

The normal CD4 count in a healthy adult us between 600 and 1500 cells/mm^3 of blood. When the CD4 count of an adult fall below 200 cells/mm^3, the risk of opportunistic and serious infection is very high (Sokomba and Gyang, 2006).

2. Method

The same method described in (Nwaozuzu et al., 2013) was also used in this study. This is part 2 of 4 from this study. The patients classified as 'improved CD4 counts' are those whose CD4 counts increased by 50 cells / mm^3 or more while those classified as 'decreased CD4 count' are those whose CD4 counts decreased by as much as 1 cell/mm^3 of blood. Those whose CD4 counts did not decrease or increase by up to 50 cells/mm^3 of blood were classified as having 'stable CD4 counts'. Those who didn't do their CD4 count test were classified as 'indeterminate'.

Before the study, an application for ethical approval of the study was sent to the management of the medical centre used for the study and the approval was granted. The components of the American society of health-system pharmacists (ASHP) guidelines on 'standardized method for pharmaceutical care' was used as a data collection instrument to evaluate, document and intervene in the antiretroviral therapy of about one thousand four hundred and seventy three (1,473) patients.

Data was collected from the patients' prescription sheets, laboratory report forms, care/ART cards, and other relevant forms in their treatment folders. Other relevant information was also obtained from the patients through oral interview. The data collected at this stage formed the base-line/ pre - intervention data for the study.

After documentation of these base-line data, pharmaceutical care interventions was implemented where necessary and this included

1. Patient education using a validated educational material applied uniformly to all the patients in the study.
2. Healthcare personnel education, counseling and discussions.
3. Recommendations for changes of drugs/regimens change of drug dose interval, duration or dosage form, addition of more drugs, treatment of untreated conditions, implementation of non-drug therapy, patient referral.
4. Ensuring that patients do their laboratory tests.
5. Monitoring the laboratory test results and carrying out interventions where necessary.

6. Giving patients access to pharmacists any time they needed it i.e. maintaining constant communication between the patients and the pharmacists.

Then a repetition of the data collection and documentation above was done nine (9) months after the implementation of the pharmaceutical care interventions mentioned above. This data represents the post - intervention data. The two data sets (baseline / pre-intervention & post-intervention data) were then be collated, analyzed and compared to see if the interventions resulted in any significant differences in the occurrence of drug therapy problems.

Appropriate statistical analysis was also applied to the data using Microsoft Excel and SPSS tools. Inclusion and exclusion criteria used for the study were;

1. New patients were excluded from the study since they will have had no previous encounter with the system and so no existing data on them.
2. Patients selected were those who have received treatment, drugs and counseling from the hospital for at least nine (9) months (i.e. who have visited the hospital for at least three (3) times).
3. Both adults and children as well as males and females were involved in the study.
4. Patients whose medications will last for less than three (3) months will be excluded from the study. This is to give the interventions enough time to make impacts and produce the possible results and to ensure uniformity of treatment duration and contact with the pharmacist in all the participating patients.

3. Results

The results showed that that 55.2% of the patients recorded significant increases in their CD4 cells count, 14.1% of them maintained their pre - intervention CD4 cells count while 10.3% of them recorded decreases in their CD4 cell count. However, in 20.4% of the patients the CD4 cell counts could not be determined. These results and other information from the study are shown in the tables below;

Table 1. Age distribution

Age Range	**Number of Patients**		Difference (A – B)	% of total = A or B/T x 100
	Pre - intervention evaluation (A) (% of total)	Post - intervention evaluation (B) (% of total)		
2 yrs – 15 yrs	146	146	0	10
15 yrs above	1327	1327	0	90
Total (T)	1473	1473	0	100

Table 1 shows that 90% of patients involved in the study were adults (18years and above) while 10% of the patients were children (2yrs – 15yrs).

Table 2. Sex (gender) distribution

sex	Number of Patients		Difference (A - B)	% of total = A/T or B/T x 100
	Pre - intervention evaluation (A) (% of total)	Post - intervention evaluation (B) (% of total)		
Male	513	513	0	35
Female	960	960	0	65
Total (T)	1473	1473	0	100

Table 2 shows that most of the patients in the study were females (65%) while the male patients accounted for 35% of the study population.

Table 3. Distribution of CD4 cell count measurement

VARIABLE	N0 OF PATIENTS	% OF TOTAL N0 OF PATIENTS EVALUATED
Increased CD4 Count	813	55.2
Stable CD4 Count	207	14.1
Decreased CD4 Count	152	10.3
Indeterminate	301	20.4
Total	1473	100

Table 3 shows that 55.2% of the patients recorded increases in their CD4 cells count, 14.1% of them maintained their pre - intervention CD4 cells count while 10.3% of them recorded decreases in their CD4 cell count. However, in 20.4% of the patients the CD4 cell counts could not be determined.

4. Statistical analysis

Hypothesis

H_0: Pharmaceutical care interventions do not improve the therapeutic outcome (CD4 count) of antiretroviral drug therapy.

H_a: Pharmaceutical care interventions improve the therapeutic outcome (CD4 count) of antiretroviral drug therapy.

Here we use table 3 shown below for statistical analysis using the Pearson's chi square (goodness of fit) test to validate the result of the foregoing study.

VARRIABLE	N0 OF PATIENTS	% OF TOTAL
Increased CD4 count	813	55.2
Stable CD4 count	207	14.1
Decreased CD4 count	152	10.3
Indeterminate	301	20.4
Total	1473	100

Here the expected frequency (Fe) is 50/50 because the chance probability is half (1/2) since we are looking at two groups of patients in the table. These are those who gave good CD4 count results (i.e. those with increased CD4 count (813) and those with stable CD4 count (207) as against those who gave bad CD4 count results (those with decreased CD4 count (152). This table above is adjusted thus,

VARRIABLE	NO OF PATIENTS	% OF TOTAL
Good CD4 Result	1020	95
Bad CD4 Result	152	5
Total	1172	100

As such,

$$X^2cal = \frac{[F_o - F_e]^2}{F_e}$$

where Fo = Observe frequency

Fe = Expected frequency

Thus,

$$X^2cal = \frac{(1020 - 50)^2}{50} + \frac{(152 - 50)^2}{50} = 18{,}818 + 208.08 = 19{,}026$$

Now, degree of freedom (Df) = (R – 1) (C – 1)

= (2 – 1) (2 – 1)

= (1) (1)

= 1

Then from Chi-square table,

Df 1 at 95% confidence level = 3.84

Thus, we now have

X^2 cal = 19,026 and

X^2 tab = 3.84

Therefore based on our decision rule, we reject Ho and accept Ha since X^2 cal > X^2 tab and conclude that Pharmaceutical care interventions improve the therapeutic outcome of antiretroviral drug therapy.

5. Discussion

CD4 Cells are a type of white blood cells that fights infections. They are also called T-helper cells. They are made in the spleen, lymph nodes and thymus gland, which are part of the infection-fighting system. CD4 cells move throughout the body, helping it to identify and destroy germs such as bacteria and viruses (Johnson, 2012). CD4 counts measures the number of CD4 cells in a sample of blood drawn by a needle from a vein in the arm. Along with other tests, the CD4 count helps tell how strong the immune system is, indicates the stage of your HIV disease, guides treatment and predicts how HIV infection/ disease may progress. Keeping the CD4 count high can reduce complications of HIV disease and prolong the patient's life.

The normal CD4 count of a healthy individual is between 500 and 1500 cells per cubic milliliter of blood. However the test does not always correspond with how well a patient is feeling. Some people can have high CD4 counts and do poorly while others can have low CD4 counts and have few complications.

Antiretroviral medications are usually started when the CD4 counts is less than 200 cells/mm^3 of blood. The fore – going study showed a positive impact of pharmaceutical care interventions on the CD4 counts (therapeutic outcome) in 95% of the patients whose CD4 counts were obtained. Only 5% of these patients experienced a decrease in their CD4 counts. These decreases were mainly due to ill – health of the patients and poor adherence to their medications. The Pearson chi - square analysis / test of goodness fit of the results showed high levels of significance of this positive impact at p value of 0.5. The lack of CD4 count results for some patients were due to many factors including ill health of some patients (which made them unable to keep their laboratory appointments), lack of transport money to the hospital (many of them come from long distances to avoid their friends and relatives knowing they are infected with HIV so as to avoid being stigmatized), inability to sneak out of their offices to keep their laboratory appointments (since they don't want their office colleagues to know about their infection so as to avoid stigmatization), frequent breakdown of the CD4 machine in the hospital and lack of seriousness of some patients with laboratory investigations amongst other reasons. These factors need to be addressed in the interest of the patients'

safety and the monitoring of their drug therapy to ensure optimal treatments and outcomes especially since CD4 count is the most affordable and readily available means of measuring therapeutic outcome of antiretroviral therapy in developing countries like Nigeria. The other laboratory investigations involved these patients' treatment also suffered the same fate of neglect.

These observations together with the results of this study further underscore the need and relevance of pharmaceutical care and the imperative of its total implementation in hospital pharmacy practice (and in other areas of pharmacy practice too), not only in the care of HIV patients but also in the care all classes of patients.

6. Conclusion

The study showed that pharmacists' interventions in antiretroviral drug therapy through Pharmaceutical care can significantly improve the CD4 cell counts of patients receiving antiretroviral drugs hence the therapeutic outcome of antiretroviral drug therapy.

7. Recommendations

- The need for initial and regular laboratory investigations need to be more emphasized and enforced before patients commence or continue their treatment.
- The role of the pharmacist in patient counseling, drug therapy monitoring and prevention/control of potential DTPs should be given more recognition and encouragement. Also specialist training of pharmacists in these areas should be embarked on.
- To be able to achieve the laudable goals of healthcare, adequate manpower should be made available. As such governments should make effort to train and employ more healthcare workers especially pharmacists whose numbers in hospitals are too small compared to the number of patients that need their attention. Pharmaceutical is both capital and manpower intensive.
- Again, efforts should be made to equip our hospitals with more current facilities to enhance the quality of care in our hospitals.

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- The intern pharmacists, Pharm Damian Obiora, Pharm Cynthia Ozurumba and Pharm John Uzoma who assisted in the course of this study. We will not forget your help.
- Federal medical centre Owerri, Imo state, Nigeria (my birth and work place) for the permission to carry out this study and many other studies there and for always encouraging us the staff to carry out research studies.

- My numerous patients who endured many months of questioning, examinations and counseling. We appreciate your patience and sacrifice. It was all for your good and better health.

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Appendix A. Ethical approval for the study

FEDERAL MEDICAL CENTRE, OWERRI

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Prof. Ivara Ejemot Esu
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Head of Administration Services
Mrs. Nnenna Onyegbula
BSc, MPA, AHAN

Head of Clinical Services
Dr. E. C. Osuagwu
M.B;B.S, FWACS
CHIEF CONSULTANT OBST. & GYNAE

23rd November, 2009

FMC/OW/HCS.11/114

Pharm. Nwaozuzu Ezeudo
Pharmacy Department
Federal Medical Centre
Owerri.

RE: PERMISSION TO CARRY OUT RESEARCH ON THE IMPACT OF PHARMACEUTICAL CARE IN THE MANAGEMENT OF PATIENTS ON ANTIBIOTICS (ANTI-INFECTIVE) THERAPY.

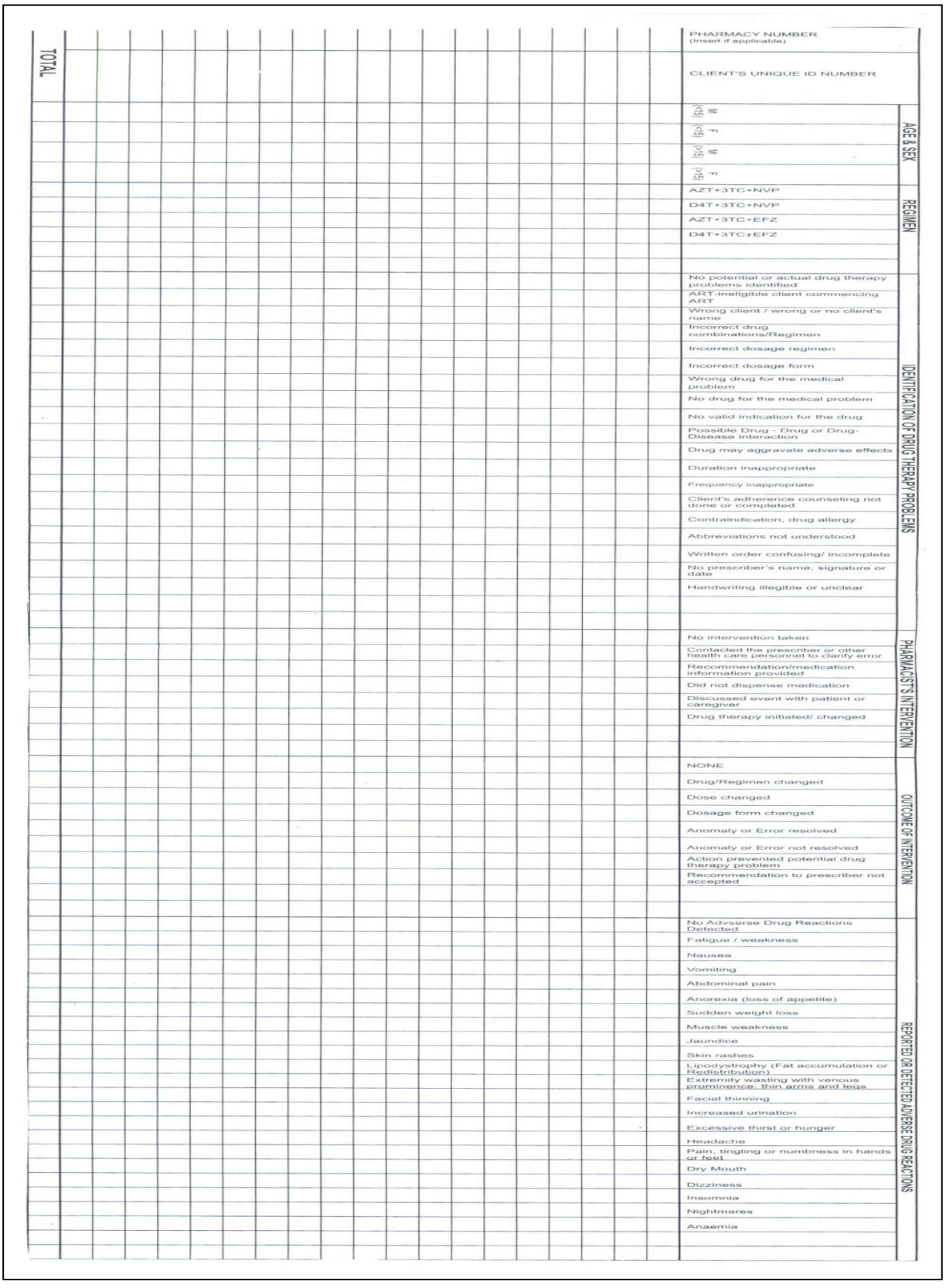
The Ethical committee acknowledges receipt of your research proposal dated 10th July 2009.

Following a meeting of the Committee held on 30th October, 2009, you have been given permission to carry out the said research.

You are also to ensure patients' confidentiality in this regard.

DR. E.C. OSUAGWU
HEAD OF CLINICAL SERVICES/CHAIRMAN ETHICAL COMMITTEE

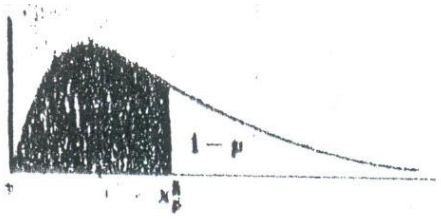
Appendix A. Data collection form



Appendix C. Chi – square distribution table

APPENDIX C

Percentile Values (χ^2_p) for the Chi-Square Distribution with ν Degrees of Freedom



ν	$\chi^2_{.005}$	$\chi^2_{.01}$	$\chi^2_{.025}$	$\chi^2_{.05}$	$\chi^2_{.10}$	$\chi^2_{.25}$	$\chi^2_{.50}$	$\chi^2_{.75}$	$\chi^2_{.90}$	$\chi^2_{.95}$	$\chi^2_{.975}$	$\chi^2_{.99}$	$\chi^2_{.995}$	$\chi^2_{.999}$
1	.0000	.0002	.0010	.0039	.0158	.102	.455	1.32	2.71	3.84	5.02	6.63	7.88	10.8
2	.0100	.0201	.0506	.103	.211	.575	1.39	2.77	4.61	5.99	7.38	9.21	10.6	13.8
3	.0717	.115	.216	.352	.584	1.21	2.37	4.11	6.25	7.81	9.35	11.3	12.8	16.3
4	.207	.297	.484	.711	1.06	1.92	3.36	5.39	7.78	9.49	11.1	13.3	14.9	18.5
5	.412	.554	.831	1.15	1.61	2.67	4.35	6.63	9.24	11.1	12.8	15.1	16.7	20.5
6	.676	.872	1.24	1.64	2.20	3.45	5.35	7.84	10.6	12.6	14.4	16.8	18.5	22.5
7	.989	1.24	1.69	2.17	2.83	4.25	6.35	9.04	12.0	14.1	16.0	18.5	20.3	24.3
8	1.34	1.65	2.18	2.73	3.49	5.07	7.34	10.2	13.4	15.5	17.5	20.1	22.0	26.1
9	1.73	2.09	2.70	3.33	4.17	5.90	8.34	11.4	14.7	16.9	19.0	21.7	23.6	27.9
10	2.16	2.56	3.25	3.94	4.87	6.74	9.34	12.5	16.0	18.3	20.5	23.2	25.2	29.6
11	2.60	3.05	3.82	4.57	5.58	7.58	10.3	13.7	17.3	19.7	21.9	24.7	26.8	31.3
12	3.07	3.57	4.40	5.23	6.30	8.44	11.3	14.8	18.5	21.0	23.3	26.2	28.3	32.9
13	3.57	4.11	5.01	5.89	7.04	9.30	12.3	16.0	19.8	22.4	24.7	27.7	29.8	34.5
14	4.07	4.66	5.63	6.57	7.79	10.2	13.3	17.1	21.1	23.7	26.1	29.1	31.3	36.1
15	4.60	5.23	6.26	7.26	8.55	11.0	14.3	18.2	22.3	25.0	27.5	30.6	32.8	37.7
16	5.14	5.81	6.91	7.96	9.31	11.9	15.3	19.4	23.5	26.3	28.8	32.0	34.3	39.3
17	5.70	6.41	7.56	8.67	10.1	12.8	16.3	20.5	24.8	27.6	30.2	33.4	35.7	40.8
18	6.26	7.01	8.23	9.39	10.9	13.7	17.3	21.6	26.0	28.9	31.5	34.8	37.2	42.3
19	6.84	7.63	8.91	10.1	11.7	14.6	18.3	22.7	27.2	30.1	32.9	36.2	38.6	43.8
20	7.43	8.26	9.59	10.9	12.4	15.5	19.3	23.8	28.4	31.4	34.2	37.6	40.0	45.3
21	8.03	8.90	10.3	11.6	13.2	16.3	20.3	24.9	29.6	32.7	35.5	38.9	41.4	46.8
22	8.64	9.54	11.0	12.3	14.0	17.2	21.3	26.0	30.8	33.9	36.8	40.3	42.8	48.3
23	9.26	10.2	11.7	13.1	14.8	18.1	22.3	27.1	32.0	35.2	38.1	41.6	44.2	49.7
24	9.89	10.9	12.4	13.8	15.7	19.0	23.3	28.2	33.2	36.4	39.4	43.0	45.6	51.2
25	10.5	11.5	13.1	14.6	16.5	19.9	24.3	29.3	34.4	37.7	40.6	44.3	46.9	52.6
26	11.2	12.2	13.8	15.4	17.3	20.8	25.3	30.4	35.6	38.9	41.9	45.6	48.3	54.1
27	11.8	12.9	14.6	16.2	18.1	21.7	26.3	31.5	36.7	40.1	43.2	47.0	49.6	55.5
28	12.5	13.6	15.3	16.9	18.9	22.7	27.3	32.6	37.9	41.3	44.5	48.3	51.0	56.9
29	13.1	14.3	16.0	17.7	19.8	23.6	28.3	33.7	39.1	42.6	45.7	49.6	52.3	58.3
30	13.8	15.0	16.8	18.5	20.6	24.5	29.3	34.8	40.3	43.8	47.0	50.9	53.7	59.7
40	20.7	22.2	24.4	26.5	29.1	33.7	39.3	45.6	51.8	55.8	59.3	63.7	66.8	73.4
50	28.0	29.7	32.4	34.8	37.7	42.9	49.3	56.3	63.2	67.5	71.4	76.2	79.5	86.7
60	35.5	37.5	40.5	43.2	46.5	52.3	59.3	67.0	74.4	79.1	83.3	88.4	92.0	99.6
70	43.3	45.4	48.8	51.7	55.3	61.7	69.3	77.6	85.5	90.5	95.0	100	104	113
80	51.2	53.5	57.2	60.4	64.3	71.1	79.3	88.1	96.6	102	107	113	116	125
90	59.2	61.8	65.6	69.1	73.3	80.6	89.3	98.6	108	113	118	124	128	137
100	67.3	70.1	74.2	77.9	82.4	90.1	99.3	109	118	124	130	136	140	149

Source: E. S. Pearson and H. O. Hartley, *Biometrika Tables for Statisticians*, Vol. 1 (1966), Table 8, pages 137 and 138.