

The continued ageing of people with AIDS in Italy: recent trend from the national AIDS Registry

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Abstract

Introduction. In industrialized countries, the availability of highly active antiretroviral therapy (HAART) caused a slow but substantial ageing of the AIDS epidemic mainly due to the longer survival of persons with HIV/AIDS which has turned HIV into a manageable, chronic disease. The number of older people with AIDS is growing in many European countries.

We described the impact of AIDS among persons aged 50 years or more in Italy and compared the characteristics of these cases with those of persons diagnosed with AIDS at an age younger than 50.

Methods. The source of data was the Italian AIDS Registry, from 1982 to 2011. We defined "older" persons those aged 50 years or more, and younger individuals those aged less than 50 years. We built two multivariate logistic regression models: the first one to identify factors associated with being older, and the second one to identify AIDS-defining diseases correlated with being older. Variables with a P value of < 0.05 were entered in the model.

Results. Of the total AIDS cases, 10.5% were among persons older than 49 years. This proportion progressively increased from 0.0% in 1983 to 26.4% in 2011. Among older cases, the incidence of AIDS was 2.0 per 100 000 residents in 1996, then decreased to 1.4 per 100 000 in 2000 and levelled off around 1 per 100 000 residents until 2011. Compared to younger cases, older cases were more frequently males, Italians, diagnosed with AIDS in recent years, residing in Northern or Central Italy, non-injecting drug users, and late testers.

Discussion. These findings stress the need for physicians to consider carefully the possibility of HIV infection among older individuals not to miss the opportunity to deliver prevention messages, offer HIV testing, and make an early diagnosis.

Key words

- AIDS
- older people
- epidemiology

INTRODUCTION

In Europe, the number of older people with AIDS is growing. The European Centre for Disease Prevention and Control (ECDC) reported an increase in the proportion of AIDS cases older than 50 years over the last fifteen years; from 9.7% in 1995 to 14.8% in 2011 [1, 2].

In industrialized countries, the availability of highly active antiretroviral therapy (HAART) caused a slow but substantial ageing of the AIDS epidemic [3, 4] mainly due to the longer survival of persons with HIV/AIDS which has turned HIV into a manageable, chronic disease.

The older patient with HIV infection is characterized by a faster progression to AIDS events and death [5-7], a faster reduction of CD4+ lymphocytes

[8], a higher frequency of comorbidities [9, 10], an increased rate of hospitalization [11], and a higher frequency of death from non-HIV-related causes (cardiovascular events 22%, liver diseases 22%, tumors 12%, other causes 44%) [12]. Persons who are diagnosed with HIV infection at older age are more frequently in an advanced clinical stage or at the onset of opportunistic diseases [7-13], and show a risk of death 2.4 times higher than those diagnosed at younger age [14].

The objective of the present study is to describe the impact of AIDS among persons aged 50 or more in Italy and to compare the characteristics of these cases with those of persons diagnosed with AIDS at an age younger than 50.

METHODS

The source of data for the present analysis is the Italian AIDS Registry, which was initiated in 1982. AIDS diagnosis is based on the criteria established by the European AIDS case definition [15]. For every AIDS case, the following individual information is recorded: socio-demographic characteristics, AIDS-defining disease (up to six diseases can be recorded for every person), mode of HIV transmission, CD4 count, HIV viral load, date of first HIV positive test (collected since 1996), antiretroviral therapy and/or prophylaxis at any time before AIDS diagnosis (collected since 1999). The coverage of the AIDS registry is national.

Usually persons aged 50 years or more are not considered as "old". However, this age cut-off is used by the Centers for Disease Control and Prevention (CDC) when analyzing data on HIV/AIDS [1-16]. In the present study, older individuals were defined as those aged 50 years or more, and younger individuals as those aged less than 50 years.

"Late testers" were defined as those persons who had their first positive HIV test result six months or less before AIDS diagnosis [17]. The characteristics of older individuals were compared with those of younger individuals using the Chi-square test.

We built two multivariate logistic regression models: the first one to identify factors associated with being older, and the second one to identify AIDS-defining diseases correlated with being older. Variables with a P value of < 0.05 were entered in the model. The statistical analysis was conducted using IBM SPSS 20.0.

RESULTS

Between 1982 and 2011, 63 891 AIDS cases were reported to the National AIDS Registry: 3530 (5.5%) were aged \leq 24 years, 53 716 (85.1%) were aged 25-49 years, 6645 (10.5%) were older than 49 years.

Among people aged \leq 24 years the incidence of AIDS reached a maximum of 1.9 per 100 000 residents in 1989 and then slowly decreased to 0.2 per 100 000 residents in 2011. Among people aged 25-49 years, the incidence peaked to 24.4 per 100 000 residents in 1995 and then decreased to 2.5 per 100 000 residents in 2011. Among persons older than 49 years, the incidence of AIDS was 2.0 per 100 000 residents in 1996, then decreased to 1.4 per 100 000 in 2000 and levelled off around 1 per 100 000 residents until 2011 (Figure 1).

Among all reported AIDS cases, the proportion of people aged \leq 24 years decreased from 12.5% in 1983 to 3.0% in 2011, whereas the proportion of people aged 25-49 years slightly decreased from 75.0% in 1983 to 70.7% in 2011 and the proportion of older people progressively increased from 0.0% in 1983 to 26.4% in 2011, and (Chi square test for trend $p < 0.001$) (Figure 2).

Among the 57 246 cases younger than 50 years of age, 76.3% were males and 9.4% were non-nationals. Overall, their median age was 33 years (IQR 29-39), increasing from 33 years in 1983 to 40 years in 2011. Thirty-three-thousand-one-hundred-sixteen (57.9%) younger cases were diagnosed in Northern Italy, 12 372

(21.6%) in Central Italy, 10 095 (17.6%) in Southern Italy, and 1614 (2.8%) reported other or undetermined risk factor. Fifty-eight percent were IDU, 18.9% were HET, 14.0% were MSM and 8.9% reported other or undetermined risk factors.

Among the 6645 older AIDS cases, 85.5% were males and 4.9% were non-nationals; the median age was 56 years (IQR 52-62) and remained stable over the years. Three-thousand-nine-hundred-and-eight (58.8%) older AIDS cases were diagnosed in Northern Italy, 1675 (25.2%) in Central Italy, 906 (13.6%) in Southern Italy; for 156 persons (2.3%) this information was missing.

Heterosexuals (HET) accounted for 40.5% of the total, 30.2% were men who have sex with men (MSM), 22.3% reported other or undetermined risk factor, and 7.0% were injecting drug users (IDU).

Compared to younger cases older cases were more frequently males, Italians, diagnosed with AIDS in recent years, residing in Northern or Central Italy, non-IDUs, and late testers ($p \leq 0.000$) (Table 1).

Among younger cases 58.3% were IDU, 18.9% were HET, 14.0% were MSM and 8.9% reported other or unknown risk factors. The proportion of IDU increased from 12.5% in 1983 to 74.0% in 1988 and then decreased to 19.5% in 2011, the proportion of HET decreased from 50.0% in 1983 to 0.0% in 1984 and then increased to 46.8% in 2011, whereas the proportion of MSM decreased from 50.0% in 1983 to 11.2% in 1993 and then increased again to 26.3% in 2011.

Among older AIDS cases 40.5% were HET, 30.2% were MSM, 22.3% reported other or undetermined risk factor and 7.0% were IDU. The proportion of IDU increased from 0.0% in 1983 to 12.3% in 2011, the proportion of HET increased from 0.0% in 1983 to 51.5% in 2011, whereas the proportion of MSM decreased from 75.0% in 1983 to 22.5% in 2011.

Since 1996 when the date of the first HIV-positive test was collected, 28 402 cases were classified as late testers. Among younger cases, 39.8% were late testers, compared to 66.7% among older persons. Among younger cases the proportion of late testers increased from 17.9% in 1996 to 61.1% in 2011, whereas among older cases the proportion of late testers was stable over the years (65-70%), (χ^2 for trend 0.000, data not shown).

Among younger cases the proportion of late testers among IDU, MSM and HET was 13.5%, 57.4%, 63.9%, respectively; among older cases the proportion of late testers among IDU, MSM and HET was 20.1%, 66.1% and 72.3%, respectively (χ^2 for trend 0.000, data not shown).

The three most frequent AIDS-defining diseases both among older and younger cases were: *Pneumocystis jirovecii* pneumonia, candidiasis of esophagus, and wasting syndrome.

However, compared to younger cases, older cases had a significantly higher risk of being diagnosed with any of the following conditions: AIDS dementia complex, wasting syndrome, immunoblastic lymphoma, recurrent pneumonia, candidiasis of bronchi, trachea, or lungs, candidiasis of esophagus, Cytomegalovirus disease; however had a significantly lower risk of presenting disseminated tuberculosis, Mycobacteriosis due to

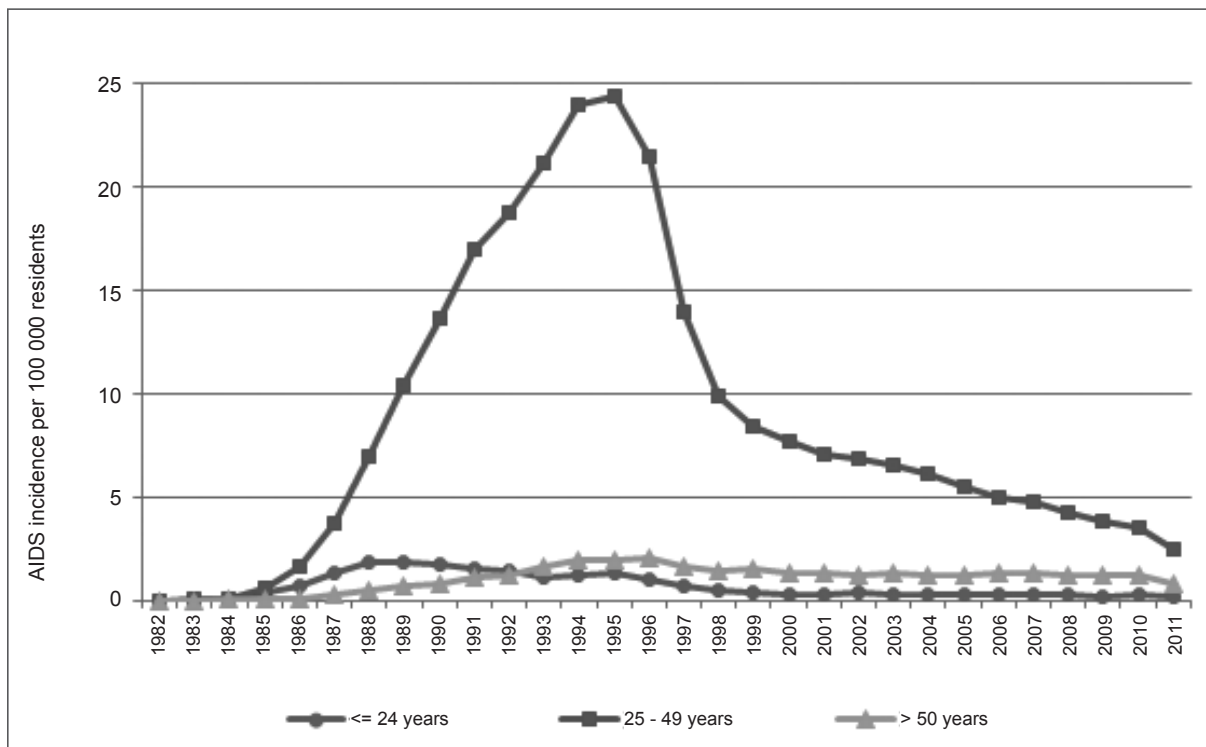


Figure 1
AIDS Incidence by age group.

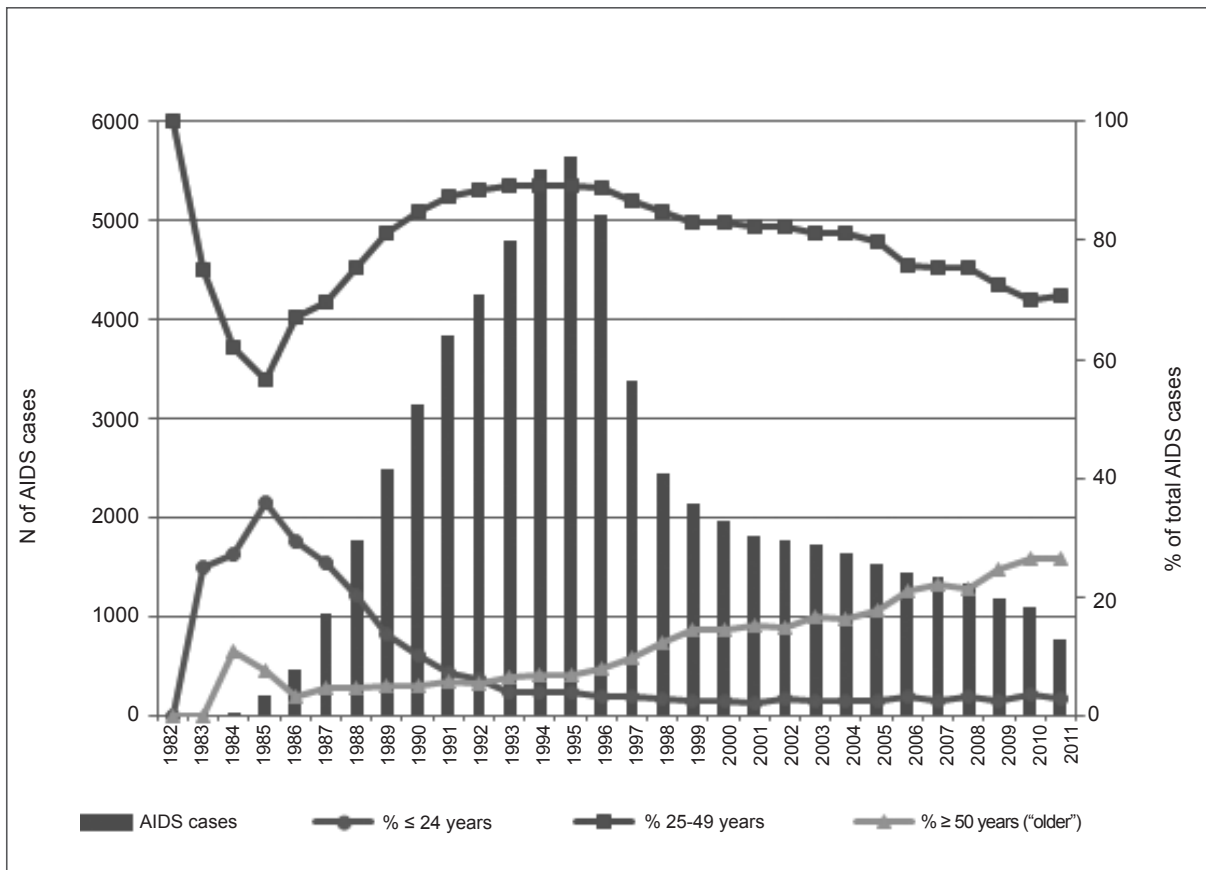


Figure 2
Annual number of incident AIDS cases and percentage of AIDS cases by age group and year.

Mycobacterium (other species), pulmonary tuberculosis, *Mycobacterium avium* complex (Table 2).

DISCUSSION

In Italy, the number of people in late adulthood with a new AIDS diagnosis is constantly increasing since 1987. In fact, in the past thirty years, the proportion of persons aged 50 years or older has tripled. A similar increase has been reported also by other European

countries [1]. The ageing of the Italian AIDS cases has been previously described [18] and can be probably attributed to the delayed progression to AIDS due to effective antiretroviral therapy [3, 4] and to the increase in the median age at HIV acquisition: the age at first HIV diagnosis, increased from 25 years in 1985 to 36 years in 2011 [19].

The incidence of AIDS showed marked decrease among people aged ≤ 24 years after 1989, and among

Table 1

Socio-demographic characteristics of older (≥ 50 years of age) and younger (< 50 years of age) incident AIDS cases. Italy 1982-2011

	Older (≥ 50 years)		Younger (< 50 years)		p	AOR (95% CI)
	n.	row %	n.	row %		
Total	6645	10.4	57 246	89.6		
Gender						
male	5679	11.5	43 668	88.5	$\leq 0.000^{**}$	2.38 (2.20-2.58)
female	966	6.6	13 578	93.4		1
Median age at diagnosis (years)	56	(IQR 52-52)	33	(IQR 29-39)	0.000*	
Nationality					$\leq 0.000^{**}$	
Italian	6320	10.9	51 848	89.1		6.02 (5.32-6.82)
Non-national	325	5.7	5392	94.3		1
missing		0.0	6	100.0		
Year of diagnosis***					$\leq 0.000^*$	1.08 (1.07-1.09)
Residence area					$\leq 0.000^{**}$	
North	3908	10.5	33 165	89.5		1.51 (1.40-1.64)
Centre	1675	11.9	12 372	88.1		1.43 (1.30-1.57)
South	906	8.2	10 095	91.8		1
Undetermined	156	8.8	1614	91.2		1.56 (1.28-1.90)
Transmission mode					$\leq 0.000^{**}$	
IDU: injecting drug user	462	1.4	33 353	98.6		1
MSM: man who have sex with man	2007	20.1	7988	79.9		14.24 (12.79-15.84)
HET: heterosexual	2692	20.0	10 801	80.0		18.48 (16.60-20.59)
other/undetermined	1484	22.5	5104	77.5		23.11 (20.67-25.84)
Late testers (available after 1996, n. = 28402)	4265		24 137		$\leq 0.000^{**}$	
First HIV-positive test ≤ 6 months before AIDS diagnosis	2846	22.8	9618	77.2		1.27 (1.17-1.37)
First HIV-positive test > 6 months before AIDS diagnosis	1419	8.9	14 519	91.1		1

* U Mann-Whitney test; ** Chi² test; *** continuous variable: OR for one-year increment in year of diagnosis.

people aged 25-49 years after 1995. A similar decrease is not evident among older AIDS cases: after the peak observed in 1996, the AIDS incidence showed a relatively stable trend over time suggesting that older people have not been reached by information prevention at younger age. Moreover, the increased time between HIV and AIDS diagnosis due to HAART therapy could determine more AIDS incident cases at more advanced age.

Italian persons with AIDS have a higher probability of being older than non-nationals. This is consistent with the fact that non-nationals living in Italy are generally younger than Italians [20] and the median age at HIV diagnosis among non-nationals is lower than that among Italians [19-21].

The finding that AIDS cases residing in Northern and Central Italy were more likely of being older than those residing in Southern Italy reflects both the age distribution of the Italian population at large, which is older in the North than in the South, and the North-South decreasing gradient of AIDS incidence [19] observed since the beginning of the epidemic.

The most common transmission modes for older cases were HET and MSM, accounting for nearly 3/4 of all older cases, whereas more than half of younger cases reported use of injecting drugs as primary transmission mode. Many older adults are sexually active and thus are as susceptible as younger persons to acquiring HIV through sexual transmission [22]. Moreover, older persons who improve sexual performance by us-

Table 2AIDS-defining diseases among older (≥ 50 years of age) and younger (< 50 years of age) AIDS cases. Italy 1982-2011

	Older		Younger		AOR (95% IC)
	Number of cases with disease	% row	Number of cases with disease	% row	
<i>Pneumocystis jirovecii</i> pneumonia	1722	10.88	14 098	89.12	1
Candidiasis of esophagus	1437	9.26	14 089	90.74	1.30 (1.20-1.41)
Wasting syndrome	876	13.72	5511	86.28	1.70 (1.54-1.87)
Toxoplasmosis of brain	441	7.45	5478	92.55	0.81 (0.72-0.90)
AIDS dementia complex	690	12.69	4748	87.31	1.85 (1.66-2.05)
Kaposi sarcoma	663	16.88	3265	83.12	1.09 (0.98-1.21)
Cytomegalovirus disease	544	18.09	2464	81.91	1.27 (1.13-1.42)
Disseminated tuberculosis	181	6.81	2475	93.19	0.55 (0.46-0.65)
Extrapulmonary Cryptococcosis	267	10.44	2291	89.56	1.01 (0.87-1.17)
Pulmonary Tuberculosis	199	8.32	2194	91.68	0.66 (0.56-0.78)
Immunoblastic lymphoma	351	16.92	1723	83.08	1.64 (1.43-1.89)
Cytomegalovirus retinitis	171	8.88	1755	91.12	0.93 (0.78-1.11)
Recurrent pneumonia	157	9.09	1570	90.91	1.45 (1.20-1.76)
Progressive multifocal leukoencephalopathy	137	9.21	1351	90.79	1.07 (0.88-1.31)
Chronic intestinal cryptosporidiosis	102	7.93	1184	92.07	0.82 (0.66-1.02)
<i>Mycobacterium</i> (other species)	83	6.49	1195	93.51	0.62 (0.49-0.79)
<i>Mycobacterium avium</i> complex or <i>Mycobacterium kansasii</i>	86	7.10	1126	92.90	0.77 (0.60-0.97)
Candidiasis of bronchi, trachea, or lungs	111	10.87	910	89.13	1.47 (1.17-1.83)
Herpes simplex	83	8.23	925	91.77	0.97 (0.76-1.24)
Burkitt lymphoma	130	18.54	571	81.46	1.18 (0.96-1.46)
Recurrent <i>Salmonella</i> septicemia	36	7.61	437	92.39	1.02 (0.71-1.48)
Primary lymphoma of brain	31	9.84	284	90.16	0.87 (0.59-1.30)
Invasive cervical cancer	10	3.68	262	96.32	0.72 (0.37-1.38)
Lymphoid interstitial pneumonia	0	0.00	168	100.00	nc
Chronic intestinal isosporiasis	9	6.00	141	94.00	0.32 (0.16-0.63)
Bacterial infections, multiple or recurrent	0	0.00	131	100.00	nc
Disseminated histoplasmosis	1	2.94	33	97.06	0.14 (0.02-1.01)
Disseminated coccidioidomycosis	3	15.00	17	85.00	1.66 (0.40-6.84)

Adjusted for those variables significantly associated with being older in Table 1.

ing sildenafil or similars, show a higher probability of engaging in sexual behaviors at risk [23]. Also in our data older persons with AIDS show a higher probability of not reporting sexual contacts as risk factor for having acquired HIV compared to younger persons with AIDS. This finding is confirmed by the high proportion of late testers observed among older persons with AIDS compared to younger persons reporting sexual contact as transmission mode. Furthermore, the stigma of HIV disease may be greater among older persons, creating barriers to accessing HIV testing and leading to delays in appropriate treatment [24].

Of particular interest is the finding that the proportion of IDU and heterosexuals is decreasing both among older and younger AIDS cases; in contrast, the proportion of MSM is decreasing among older but not among younger cases [1-25].

Moreover, in our analysis older AIDS cases have overall a higher probability compared to younger AIDS cases to be late testers. This is consistent with previous studies conducted in Europe and Italy showing a significantly higher proportion of older AIDS cases diagnosed at a more advanced stage of HIV infection compared to younger AIDS cases [17-26]. Several factors may contribute to the late diagnosis of AIDS in older persons. Older persons may be less aware of being at risk for HIV infection [27], probably due to the fact that prevention messages and services have historically been primarily addressed to younger age groups.

Moreover, AIDS may be misdiagnosed because some symptoms can mimic those of normal ageing, for example, fatigue, weight loss, depression, Alzheimer's disease and mental confusion [28]. In fact, our results show that older adults with AIDS had a higher probability of being diagnosed with AIDS dementia complex or wasting syndrome than younger adults with AIDS, similarly to what reported recently by CDC [29].

In conclusion, our results show that the majority of

older adults diagnosed with AIDS were predominantly Italian males, residing in Northern Italy, acquired the infection through sexual contact, and about two-thirds of them was diagnosed late. The incidence has remained stable over the last ten years.

These findings stress the need for physicians to consider carefully the possibility of HIV infection among older individuals. Health care professionals tend to underestimate the probability of HIV/AIDS among older, thus missing the opportunity to deliver prevention messages, offer HIV testing, and make an early diagnosis.

Moreover, the national health authority should consider that the increasing number of older AIDS cases deserves a new planning of health care services to increase home care, hospice care, and community care.

Older adults are seldom included in prevention programs. Information campaigns targeting older persons are required, both to prevent HIV transmission and to diagnose and treat HIV infection in a timely manner.

Author's contributions

SB managed the AIDS database, LC and VR made the data analysis and wrote the paper, MCS and MR contributed to writing the paper and BS supervised and revised the manuscript.

Acknowledgments

The authors wish to thank Lucia Pugliese for the data input.

Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

Received on 11 February 2014.

Accepted on 7 July 2014.

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