

## Respiratory symptoms and illness in older Australians: the Burden of Obstructive Lung Disease (BOLD) study

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Several recent expert summaries have highlighted the health impacts of chronic obstructive pulmonary disease (COPD).<sup>1-4</sup> In Australia, there were 4761 deaths (4% of all deaths) attributed to COPD in 2006,<sup>5</sup> and 47 207 years of life were lost due to COPD in 2003.<sup>6</sup> In 2006-07, there were 52 560 hospital separations in Australia attributed to COPD, with an average length of stay of 7 days.<sup>5</sup> COPD has a substantial impact on mortality and health service use.

Data on the prevalence of COPD and related symptoms are limited, with estimates ranging from 1.4% to 6.9%, depending on the age group studied and the definitions used.<sup>5,7,8</sup>

COPD is usually not diagnosed until it is moderately advanced and begins to impair quality of life. Furthermore, due to poor utilisation of spirometry in primary care settings<sup>9-11</sup> and the largely silent nature of the disease in its early stages, COPD is under-recognised by doctors and under-reported by patients. Surveys that have used objective measurement of lung function to identify COPD have found a high proportion of previously undiagnosed cases.<sup>12</sup>

Valid estimation of the prevalence of COPD requires a comprehensive, nationwide, population-based survey, including high-quality post-bronchodilator spirometry, conducted in a representative sample of the population.<sup>4</sup> In collaboration with the international Burden of Obstructive Lung Disease (BOLD) study,<sup>13</sup> we conducted this research to describe the prevalence of obstructive lung disease, including symptoms, diagnoses and level of airflow obstruction, in people aged 40 years or older in Australia.

### Abstract

**Objective:** To measure the prevalence of chronic obstructive pulmonary disease (COPD) among people aged 40 years or older in Australia.

**Design, setting and participants:** A cross-sectional study of people in the community aged  $\geq 40$  years, selected at random using electoral rolls, in six sites chosen to reflect the sociodemographic and geographic diversity of Australia, conducted between 2006 and 2010. Standardised questionnaires were administered by interview. Forced expiratory volume in 1 second (FEV<sub>1</sub>), forced vital capacity (FVC), and the FEV<sub>1</sub>/FVC ratio were measured by spirometry, before and after bronchodilator administration.

**Main outcome measure:** Prevalence of COPD, classified according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2006 criteria.

**Results:** Complete data were available for 1620 men (participation rate, 26%) and 1737 women (participation rate, 28%). The prevalence of GOLD Stage II or higher COPD (defined as post-bronchodilator FEV<sub>1</sub>/FVC ratio  $< 0.70$  and FEV<sub>1</sub>  $< 80\%$  predicted) was 7.5% (95% CI, 5.7%–9.4%) among people aged  $\geq 40$  years, and 29.2% (95% CI, 18.1%–40.2%) among those aged  $\geq 75$  years. Among people aged  $\geq 40$  years, the prevalence of wheeze in the past 12 months was 30.0% (95% CI, 27.5%–32.5%), and prevalence of shortness of breath when hurrying on the level or climbing a slight hill was 25.2% (95% CI, 22.7%–27.6%).

**Conclusions:** Symptoms and spirometric evidence of COPD are common among people aged 40 years or older and increase with age. Further research is needed to better understand the diagnosis and management of COPD in Australia, along with continuing efforts to prevent the disease.

### Methods

We conducted the survey in a representative sample of adults aged  $\geq 40$  years living in six locations around Australia. One centre with a large Indigenous population was included. Post-hoc weights were used to make inferences about prevalence in the entire Australian population aged  $\geq 40$  years.

The study commenced in Sydney in 2006, as part of the international BOLD study. The protocol<sup>13</sup> and main results<sup>14</sup> for Sydney have already been published, together with data from centres in 11 other countries. Data from Sydney are included here, along with data from the remaining five Australian locations. The protocol used in this study closely followed that used in the global BOLD study.

The study was approved by the Human Research Ethics Committee

of the University of Sydney (ref. no. 12-2006/9724). Additionally, all sites obtained local ethics approval. All participants gave written informed consent.

### Sampling plan and recruitment

Study participants were sampled from electoral rolls, after excluding those who were institutionalised, using a sex-stratified, simple random sample in all sites except Broome and Busselton (Appendix 1; online at [mja.com.au](http://mja.com.au)).

As many of the Aboriginal and Torres Strait Islander residents of Broome are not on the electoral roll, the sampling frame at this site was established using a household census. We then recruited a stratified random sample of Indigenous and non-Indigenous male and female residents aged  $\geq 40$  years from this sampling frame. In Busselton, we followed a two-stage

sampling strategy. A sample was recruited from the electoral roll for the Busselton Health Study,<sup>15</sup> and study participants were then selected using sex-stratified random sampling from among those who participated in the Busselton Health Study.

All selected individuals in study centres other than Broome initially received a letter inviting them to participate and, if interested, to telephone for an appointment. After 2 weeks, study staff telephoned those individuals who had not made contact and made several further attempts to contact them by telephone or mail.

Individuals who declined to participate in the study were asked to complete a brief questionnaire that included questions about age, respiratory illness and smoking status.

### Study questionnaire

We used the BOLD study questionnaire<sup>13,14</sup> without modification in all study centres, except for Aboriginal and Torres Strait Islander participants in Broome, whose first language was often not English. The questionnaire was administered by interview.

### Spirometry testing

We performed spirometry testing, using the EasyOne spirometer (nDD Medizintechnik), before and 15 minutes after administration of salbutamol 200 µg via metered dose inhaler and spacer.<sup>13</sup> Participants were asked to refrain from using their bronchodilator inhaler during the 6–12 hours before testing.

All spirometry results were reviewed by one of us (DPJ) and assigned a quality score based on published acceptability and repeatability criteria.<sup>16</sup>

### Classification of spirometric end points

The highest recorded forced expiratory volume in 1 second (FEV<sub>1</sub>) and forced vital capacity (FVC) from acceptable trials<sup>16</sup> were used in the analysis. Participants with a post-bronchodilator FEV<sub>1</sub>/FVC ratio < 0.70 were classified as having COPD based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometric criteria.<sup>4</sup> Among these, participants with FEV<sub>1</sub> ≥ 80% predicted<sup>17</sup> were classified as having

**1 Demographic characteristics of the study sample with complete data compared with the Australian population aged ≥ 40 years in the 2006 census**

	Men		Women		All	
	Sample*	Census	Sample*	Census	Sample*	Census
Age ≥ 75 years	12.7%	11.9%	10.5%	16.0%	11.6%	14.0%
Age ≥ 65 years	34.1%	27.2%	30.2%	31.0%	32.1%	29.2%
Most disadvantaged SEIFA quintile	25.4%	19.0%	25.8%	19.6%	25.6%	19.3%
Living in remote or very remote areas	16.0%	2.2%	17.0%	1.7%	16.5%	1.9%
Aboriginal or Torres Strait Islander	2.6%	1.1%	3.9%	1.2%	3.3%	1.2%

SEIFA = Socio-Economic Indexes for Areas. \* Participants who completed the core questionnaire and had acceptable post-bronchodilator spirometry data. ◆

GOLD Stage I COPD; those with FEV<sub>1</sub> ≥ 50% to < 80% predicted as GOLD Stage II; those with FEV<sub>1</sub> ≥ 30% to < 50% predicted as GOLD Stage III, and those with FEV<sub>1</sub> < 30% predicted as GOLD Stage IV. In addition, those with a post-bronchodilator increase in FEV<sub>1</sub> that was both ≥ 12% of the pre-bronchodilator FEV<sub>1</sub> and ≥ 200 mL were classified as having reversible spirometry consistent with asthma.

### Sample size estimation

The sample size at each site of 300 men and 300 women was designed to achieve a 95% confidence interval half-width of between 2.5% and 5.3% for prevalence rates ranging from 6% to 33% within each study centre.<sup>13</sup> In most centres, an initial sample of 2400 was drawn, and additional samples were drawn from the sampling frame until the required sample size was achieved.

### Post-hoc weights

As this was not a simple random sample of the Australian population aged ≥ 40 years, we used post-hoc weights to estimate prevalence rates for the Australian population after adjustment for age, sex, socioeconomic status (using Socio-Economic Indexes for Areas [SEIFA]<sup>18</sup>), remoteness (using the Accessibility/Remoteness Index of Australia [ARIA]<sup>19</sup>), and Indigenous status. SEIFA and ARIA categories were assigned to individuals by postcode of residence. Weights were calculated by comparing the distribution of the study participants according to these characteristics with the distribution of the Australian population aged ≥ 40 years, from the 2006 Australian Census of Population

and Housing, obtained from the Australian Bureau of Statistics.

### Statistical analysis

Prevalence estimates and associated 95% confidence intervals were calculated for participants who completed the core questionnaire and had acceptable post-bronchodilator spirometry data. Prevalence was estimated, taking account of the stratified nature of the sample and including the post-hoc weights, using Proc Surveyfreq (SAS 9.2; SAS Institute). Study site was the stratifying variable.

### Results

Overall, the initial study sample for all sites included 6328 men and 6198 women aged ≥ 40 years (Appendix 2; online at [mja.com.au](http://mja.com.au)). After excluding people who were known to have permanently left the study area, or who were deceased, aged < 40 years, institutionalised, or for whom a registered address did not exist, there were 5352 eligible men and 5408 eligible women. Core questionnaire and acceptable post-bronchodilator spirometry data were available for 1620 men (participation rate, 26%) and 1737 women (participation rate, 28%). After excluding individuals who were not contactable, the adjusted participation rates were 35% for men and 37% for women, for all sites except Broome. Data on age, respiratory diagnoses and smoking status were available for an additional 893 men (14% of initial population) and 1111 women (18% of initial population) who had declined to participate.

Participants who completed the core questionnaire and had acceptable post-bronchodilator spirometry

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2 Weighted prevalence of respiratory symptoms and illnesses and spirometric diagnoses, by age group and sex\*

	All ages ≥ 40 years			Age 40–54 years			Age 55–74 years			Age ≥ 75 years		
	Men	Women	All	Men	Women	All	Men	Women	All	Men	Women	All
<b>In past year</b>												
Cough on most days for ≥ 3 months	9.3 (7.0–11.6)	9.6 (7.6–11.6)	9.5 (7.9–11.0)	9.2 (6.2–12.1)	9.8 (6.6–13.0)	9.5 (7.3–11.7)	8.0 (5.6–10.5)	10.1 (7.0–13.3)	9.1 (7.1–11.1)	14.2 (1.7–26.8)	7.4 (3.2–11.7)	10.3 (4.3–16.4)
Phlegm on most days for ≥ 3 months	10.2 (7.5–12.9)	4.9 (3.4–6.3)	7.4 (5.9–9.0)	9.0 (5.9–12.0)	4.0 (2.0–6.0)	6.4 (4.6–8.3)	8.6 (6.2–11.0)	6.4 (3.8–8.9)	7.5 (5.7–9.2)	20.4 (4.3–36.5)	3.6 (0.8–6.4)	10.8 (3.0–18.5)
Wheeze	29.0 (25.6–32.5)	30.9 (27.3–34.5)	30.0 (27.5–32.5)	31.2 (25.8–36.6)	32.4 (27.4–37.5)	31.8 (28.1–35.5)	27.5 (23.2–31.7)	27.1 (22.5–31.8)	27.3 (24.2–30.4)	25.8 (13.0–38.6)	35.8 (21.9–50.0)	31.5 (21.8–41.3)
<b>Shortness of breath†</b>												
When hurrying on the level or climbing slight hill	19.4 (16.2–22.5)	30.6 (27.0–34.2)	25.2 (22.7–27.6)	14.3 (10.6–18.0)	22.6 (18.1–27.0)	18.5 (15.6–21.4)	20.7 (16.8–24.7)	31.8 (27.2–36.4)	26.3 (23.3–29.4)	36.0 (20.0–52.0)	55.0 (41.0–69.1)	46.6 (36.0–57.2)
Walks slowly due to breathlessness	3.9 (2.4–5.4)	5.8 (4.4–7.3)	4.9 (3.9–5.9)	1.6 (0.0–3.5)	4.7 (2.5–6.9)	3.2 (1.8–4.7)	5.2 (3.0–7.4)	6.0 (4.1–8.0)	5.6 (4.2–7.1)	7.5 (1.2–13.7)	8.5 (3.6–13.4)	8.0 (4.2–11.8)
Stops for breath when walking at own pace	4.4 (1.9–6.9)	5.7 (3.3–8.2)	5.1 (3.4–6.8)	1.4 (0.0–3.8)	3.1 (1.4–4.8)	2.3 (1.0–3.5)	4.0 (2.0–6.0)	5.2 (2.6–7.8)	4.6 (3.0–6.2)	16.4 (0.8–32.0)	14.7 (1.9–27.6)	15.5 (5.5–25.4)
Stops for breath after walking 100 m	3.2 (0.9–5.6)	3.0 (1.8–4.3)	3.1 (1.8–4.4)	0.05 (0.0–0.1)	1.5 (0.1–2.8)	0.8 (0.1–1.5)	2.0 (0.6–3.5)	3.2 (0.8–5.6)	2.6 (1.2–4.1)	18.2 (2.2–34.2)	7.1 (2.7–11.5)	11.8 (4.2–15.9)
Housebound due to breathlessness	1.4 (0.5–2.3)	0.6 (0.1–1.1)	1.0 (0.5–1.5)	1.0 (0.0–2.4)	0.4 (0.0–1.0)	0.7 (0.0–1.4)	1.6 (0.2–2.9)	0.4 (0.0–0.8)	1.0 (0.3–1.7)	2.4 (0.0–5.1)	1.7 (0.0–3.9)	2.0 (0.3–3.7)
<b>Ever diagnosed with</b>												
Chronic bronchitis, emphysema or COPD	5.1 (3.7–6.5)	5.3 (4.0–6.7)	5.2 (4.2–6.2)	2.3 (0.8–3.9)	4.2 (2.2–6.2)	3.3 (2.0–4.5)	7.4 (4.9–10.0)	7.0 (4.7–9.4)	7.2 (5.5–9.0)	8.4 (3.6–13.1)	4.5 (1.4–7.6)	6.2 (3.5–8.9)
Asthma, asthmatic or allergic bronchitis	16.0 (13.3–18.7)	21.5 (18.7–24.3)	18.8 (16.9–20.7)	16.8 (13.1–20.5)	24.8 (20.4–29.2)	20.9 (18.0–23.8)	14.6 (11.3–17.9)	20.3 (16.6–23.9)	17.5 (15.0–20.0)	17.3 (4.5–30.2)	14.4 (6.6–22.1)	15.6 (8.5–22.7)
Ever smoked cigarettes	54.4 (50.6–58.1)	45.5 (41.7–49.2)	49.8 (47.1–52.4)	50.1 (44.5–55.8)	49.8 (44.5–55.1)	50.0 (46.1–53.8)	59.9 (55.4–64.5)	43.2 (38.1–48.4)	51.5 (48.0–54.9)	52.3 (37.6–67.1)	37.8 (23.9–51.8)	44.0 (34.2–53.8)
<b>GOLD Stage</b>												
I or higher	15.2 (12.5–17.9)	13.9 (10.8–16.9)	14.5 (12.4–16.6)	5.8 (3.6–8.0)	6.2 (3.6–8.8)	6.0 (4.3–7.7)	20.2 (16.2–24.1)	13.3 (10.3–16.3)	16.6 (14.1–19.1)	37.8 (22.6–53.0)	41.6 (26.3–56.9)	40.0 (29.1–50.8)
II or higher	6.9 (4.7–9.1)	8.1 (5.3–11.0)	7.5 (5.7–9.4)	1.7 (0.7–2.7)	2.2 (0.6–3.9)	2.0 (1.0–3.0)	8.3 (5.5–11.1)	6.5 (4.6–8.4)	7.3 (5.7–9.0)	24.1 (9.6–38.7)	32.9 (17.1–48.7)	29.2 (18.1–40.2)
III or IV	1.2 (0.5–1.9)	0.7 (0.3–1.1)	0.9 (0.5–1.3)	0.2 (0.0–0.7)	0.0 (0.0–0.0)	0.1 (0.0–0.3)	2.1 (0.5–3.6)	1.0 (0.3–1.7)	1.5 (0.7–2.3)	2.3 (0.1–4.6)	2.0 (0.0–4.2)	2.1 (0.6–3.7)
Reversible spirometry consistent with asthma‡	8.1 (5.5–10.7)	3.7 (2.4–4.9)	5.8 (4.4–7.2)	5.5 (3.4–7.7)	3.4 (1.5–5.3)	4.4 (3.0–5.8)	7.3 (5.0–9.6)	4.1 (2.0–6.3)	5.7 (4.1–7.3)	21.2 (4.7–37.8)	3.2 (0.6–5.9)	11.1 (2.8–19.3)

COPD = chronic obstructive pulmonary disease. GOLD = Global Initiative for Chronic Obstructive Lung Disease. \*Figures are % (95% CI). †Medical Research Council Dyspnoea Scale (adapted from<sup>20</sup>). ‡Participants who reported being unable to walk due a condition other than shortness of breath are excluded from the denominator. ‡Post-bronchodilator increase in forced expiratory volume in 1 second (FEV<sub>1</sub>) that is both ≥ 12% of pre-bronchodilator FEV<sub>1</sub> and ≥ 200 mL.

data were younger and more likely to report a history of emphysema, asthma, asthmatic bronchitis, chronic bronchitis or COPD than those for whom only minimal data were available (Appendix 3; online at [mja.com.au](http://mja.com.au)). Men with complete data were less likely to have ever smoked than men with minimal data, but the reverse was the case among women. Compared with the Australian population aged ≥ 40 years, those with complete data were less likely to be aged ≥ 75 years (among women),

more likely to live in the most socio-economically disadvantaged areas and remote areas, and more likely to be Aboriginal or Torres Strait Islanders (Box 1).

The weighted prevalence of respiratory symptoms, reported clinical respiratory diagnoses and spirometric diagnoses in the study sample, classified by age group and sex, are shown in Box 2. Wheeze and shortness of breath when hurrying on the level or climbing a slight hill were common symptoms. The prevalence of cough

was similar among the age groups, but the prevalence of sputum production, consistent with a diagnosis of chronic bronchitis, increased with age. There was a steep increase in the prevalence of shortness of breath in people aged ≥ 75 years. About half the study population reported ever having smoked cigarettes. A reported diagnosis of asthma or related illness was much more common than a reported diagnosis of COPD or related illness (18.8% v 5.2% among all people aged ≥ 40 years), even in

the oldest age group. Among all people aged  $\geq 40$  years, the prevalence of GOLD Stage II or higher COPD was 7.5% and the prevalence of severe COPD (GOLD Stage III or higher) was 0.9%; prevalences were higher in the oldest age group.

## Discussion

We found that the prevalence in Australia of GOLD Stage II or higher COPD, defined by spirometric criteria, is 7.5% among people aged  $\geq 40$  years and 29.2% among people aged  $\geq 75$  years. Smaller proportions of people reported having previously received a diagnosis of COPD (including chronic bronchitis or emphysema), but much higher proportions reported breathlessness on exertion.

The prevalence of GOLD Stage II or higher COPD among 11 international sites ranged from 8.5% in Reykjavik, Iceland, to 22.2% in Cape Town, South Africa, in men; and from 3.7% in Hannover, Germany, to 16.7% in Cape Town in women.<sup>14</sup> Our estimates for Australia, 6.9% and 8.1%, respectively, therefore lie at the lower end of the international range for men and in the middle for women.

These estimates are not directly comparable with other Australian estimates of the prevalence of COPD. The 2004–05 National Health Survey reported that 2.8% of Australians aged  $\geq 18$  years self-reported a diagnosis of COPD, chronic bronchitis or emphysema.<sup>5</sup> We found that 5.2% of people aged  $\geq 40$  years reported having received these diagnoses. The difference may be attributable to the different ages of the survey populations. This may also explain why the prevalence in the Northwest Adelaide Health Study, which included people aged  $\geq 18$  years, was lower than in our study.<sup>8</sup>

The main strengths of our study are the nationwide study population, the large sample size leading to relatively precise estimates, the use of objective measures with careful attention to quality control of spirometry, and the application of standardised definitions. Harmonisation of the study protocol with a widely used international protocol allows comparison with many reference populations.

The main limitation was the poor overall response rate, which introduces the possibility of selection bias affecting the prevalence estimates. Participants who provided complete data, and hence contributed to the prevalence estimates, were slightly younger but were more likely to self-report a diagnosis of COPD than those who provided only minimal data. Although this implies that people with COPD may be overrepresented in the study sample, we do not have information on those who declined to provide any information, and we should not assume that they were similar to those who provided minimal data.

The study population was not a simple random sample of the Australian population because the six study centres were not randomly chosen. The study centres were deliberately selected to provide adequate representation of the sociodemographic and geographic diversity of Australia. Hence, rural, Indigenous and disadvantaged areas were deliberately oversampled. Post-hoc weights, based on the Australian census, were intended to simultaneously adjust for the non-random selection of sites and for bias attributable to non-response among eligible participants. This strategy adjusts for non-representativeness with respect to age, sex, socioeconomic disadvantage and remoteness. However, it is possible that there were other, unmeasured biases relevant to the prevalence of COPD.

We defined and classified COPD according to the internationally agreed GOLD guidelines<sup>4</sup> that have also been adopted by the BOLD study.<sup>13</sup> There has been substantial debate around these definitions.<sup>21–23</sup> This is because spirometric function is measured on a continuous scale, and any binary classification based on cut-points is essentially arbitrary. Lung function declines with age, and there is debate about the extent to which this is “normal” and hence should be incorporated into reference equations, and consequently used to discount the increasing prevalence of COPD in older people. We have dealt with this issue by reporting the prevalence of a range of measures, both objective and subjective, to encapsulate the spec-

trum of obstructive lung disease and related illness in the community.

The relationship between asthma and COPD in older people is complex.<sup>24</sup> In our study population, 5.8% of people had bronchodilator reversibility, which may be a feature more consistent with asthma than COPD, although it does not exclude the latter diagnosis. However, the prevalence of bronchodilator reversibility was higher in men than in women, which is the reverse of the difference in prevalence of self-reported asthma in Australia.<sup>25</sup> While asthma and COPD may coexist in individuals, it is not possible to deduce any causal relationship between them in cross-sectional studies such as this.<sup>26</sup>

The findings of our Australian BOLD study have important implications for health service development in Australia. Only by accurately diagnosing COPD is it possible to offer the range of interventions that have been demonstrated to improve quality of life, reduce disability and limit health care use. The finding that many participants with confirmed airflow obstruction consistent with COPD did not have a pre-existing diagnosis suggests greater effort is needed in making high-quality spirometry available in all health care settings. The prevalence findings will also be integral in informing the ongoing development of treatment services for people living with COPD. This includes access to smoking cessation programs, pulmonary rehabilitation, lung volume reduction and lung transplantation.

COPD is a common and serious health problem, particularly among older people, with major impacts on health resources and personal and community costs. It is often not recognised, in part because the diagnosis requires spirometry, a procedure that is not widely used in primary care.<sup>25</sup> There is a need for further research to better understand the extent to which COPD is optimally recognised and managed in Australia and for continuing efforts to prevent the disease by avoidance of smoking and improvements in ambient and occupational air quality.

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## Stamps of greatness



### Nicolaes Tulp (1593–1674)

**BORN** Claes Pieterszoon in Amsterdam on 9 October 1593, Tulp graduated with a degree in medicine from Leiden University in 1614.

When he returned to Amsterdam to practise, he adopted the tulip as his family crest and changed his name to Nicolaes Tulp.

He was a member of the Surgeon's Guild from 1628 to 1653, and became a professor of anatomy. He also served as a city councillor and mayor for several terms.

As many of his patients were sailors and merchants from the East Indies, he became one of the first to describe cases of beriberi, caused by a thiamine (vitamin B<sub>1</sub>) deficiency in the diet.

He was responsible for the publication of the first *Amsterdam pharmacopeia*.

In 1632, the guild commissioned Rembrandt to paint a group portrait of prominent councillors and guildmasters. This resulted in the famous *Anatomy Lesson of Dr Nicolaes Tulp*, which now hangs in the Mauritshuis Museum in The Hague. It depicts Tulp dissecting a criminal's forearm. The Surgeon's Guild sometimes held public anatomy lessons, where the corpse of an executed criminal was dissected before a large paying audience. (Part of the proceeds went towards hosting a lavish banquet for the surgeons.)

Some of the spectators were doctors who paid commissions to be included in the portrait, and the painting shows them appropriately dressed for such a solemn social occasion. Tulp's standing is indicated by the fact that he is the only one shown wearing a hat.

Tulp died in The Hague on 12 September 1674, and was honoured postally by Togo in 1968 and by Cameroon in 1970 as a great anatomist and surgeon.

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