RECOMMENDED CITATION
Werneck GL, Macias AE, Mascarenas C, Coudeville L, Morley D, Recamier V, et al. Comorbidities increase in-hospital mortality in dengue patients in Brazil [Submitted]. Mem Inst Oswaldo Cruz E-pub: 20 Feb 2018. doi: 10.1590/0074-02760180082.

Short Communication

Comorbidities increase dengue mortality

Comorbidities increase in-hospital mortality in dengue patients in Brazil

Guilherme L. Werneck*[#1], Alejandro E. Macias*[2], Cesar Mascarenas[3], Laurent Coudeville[3], David Morley[4], Vincent Recamier[4], Mariana Guergova-Kuras[4], Esteban Puentes-Rosas[5], Nicolas Baurin[3], Myew-Ling Toh[3]

[1]*Instituto de Estudos em Saúde Coletiva, Universidade Federal do Rio de Janeiro, Rio de Janeiro RJ, Brasil;* [2]*Área De Microbiología, Departamento De Medicina, Universidad de Guanajuato, Guanajuato, Mexico;* [3]*Sanofi Pasteur, Lyon, France;* [4]*Ariana Pharmaceuticals, Paris, France;* [5]*Sanofi Pasteur, Mexico*

*Joint first authors

[#]Corresponding author: gwerneck@iesc.ufrj.br

Abstract

Dengue remains an unmet public health burden. We determined risk factors for dengue in-hospital mortality in Brazil. Of 326,380 hospitalized dengue cases in 9–45 years old individuals, there were 971 deaths. Risk of dying was 11 times higher in the presence of underlying common comorbidities (renal, infectious, pulmonary disease and diabetes), similar to the risk of dying from severe dengue and much higher with the combination. Ensuring access to integrated dengue preventative measures in individuals ≥9 years including those with comorbidities may help achieve the WHO objective of 50% reduction in mortality, 25% reduction in morbidity to dengue by 2020.

Key words: dengue, hemorrhagic fever, Latin America, case fatality rate

Sponsorship: This study was funded by Sanofi Pasteur including service provision of database consolidation, data mining and analysis by Ariana Pharmaceuticals. Editorial assistance with the preparation of the manuscript was provided by Richard Glover and Rebecca Hornby, inScience Communications, Springer Healthcare, Chester, UK. Funding for latter assistance was also provided by Sanofi Pasteur. The authors also thank Jean-Sébastien Persico for editorial assistance and manuscript coordination on behalf of Sanofi Pasteur.

In Brazil, dengue is geographically spreading with increasing numbers of reported cases and severity. Recent surveillance data indicate that between 2010–2016 Brazil suffered an average of 1,077,025 suspected, and 245,925 laboratory-confirmed dengue cases, annually (PAHO 2017a), however the true burden is likely underestimated (Sarti et al. 2016). According to Fares *et al.* (2015), the incidence of dengue in Brazil has been frequently high, and the number of cases in the country has at some point in time represented up to 60% of the dengue reported cases worldwide (Fares et al. 2015), with significant economic costs of US$ 728 million mostly due to ambulatory dengue cases (Shepard et al. 2016).

Death rates remain high and the goal of reducing dengue case fatality rate (CFR) < 1% set by the World Health Organization (WHO) and the National Dengue Control program in Brazil remains unreached (MS 2002; WHO 1997). In Brazil, the Pan American Health Organization (PAHO) report CFRs for dengue cases range from 0.04 to 4.07% annually (Pan American Health Organization 2017b). However, CFRs as high as 18.6% were reported for dengue patients in intensive care units (ICU) and 19.6% for in-hospital patients in a recent study in Minas Gerais State in South Eastern Brazil (Amancio et al. 2015; Durand et al. 2017). As dengue CFR in Brazil may differ by two orders of magnitude from year to year, other dengue infection factors must be considered in estimating the disease severity. Comorbidities are highly prevalent in dengue endemic areas including Brazil, and contribute to some of the highest death rates and public health burden in those countries (Hotez & Peiperl 2015; Mehta & Hotez 2016). Dengue patients with comorbidities may be at higher risk of severe dengue and death, however there have been no large scale studies conducted in Brazil (Figueiredo et al. 2010; Teixeira et al. 2015; Toledo et al. 2016).

In a large retrospective cohort study, we determined risk factors for dengue in-hospital mortality from the Brazilian Hospital Information System of the Unified Health System (SIH/SUS) database over an 8 year period (2008–2015) (Ministério da Saúde). Hospital admission records (92 million) from 20,576 departments at 5,983 hospitals were included. Patient records from 326,380 hospitalized dengue cases in 9–45 years old individuals, 173,778 female (53.2%) and 152,602 male (46.8%) were analyzed. Ethical approval was not required as the database was publically accessible. In-hospital mortality was identified and dengue cases and comorbidities were identified directly from the recorded principal and secondary diagnoses for each hospitalized dengue case using the International Classification of Diseases, 10th Revision (ICD 10) codes (WHO 2014). Dengue cases were divided into either non-severe (ICD 10 code=A90; classical dengue) or severe dengue diagnosis codes (ICD 10 code=A91; dengue hemorrhagic fever).

In order to exclude potential bias in the analysis, as comorbidities may also be a consequence of severe dengue manifestations, codes considered as severe dengue symptoms and complications were excluded. The comorbidity definitions used are summarized in **Supplementary Table S1**. Analyses were performed using the KNIME (Berthold et al. 2008) analytic platform integrated with KEM® (Ariana Pharmaceuticals; Liquiere & Sallantin 1998) data mining tools, MySQL database and R v3.0.3 statistical software (Team 2011). Data was presented as CFR and relative mortality ratios (RMR) and 95% confidence intervals (CI) compared to different groups. P values on RMR were determined for statistical significance by Fisher's exact test, whereby $p < 0.05$ was considered statistically significant.

We first determined whether mortality rates were increased in hospitalized dengue patients with underlying comorbidities compared to the absence of comorbidities. Of a total of 326,380 hospitalized dengue cases in individuals 9–45 years old, there were 971 deaths in

this age group with an overall CFR of 0.30% (**Table 1**). The crude relative mortality risk (RMR) from hospitalized dengue was 11 times higher (95% CI 9–15) in the presence of common comorbidities (CFR 3.07%, p< 0.001) compared to those without comorbidities (CFR 0.27%).

The risk of dying from hospitalized dengue with underlying comorbidities (CFR 1.94%, RMR 13, 95% CI 9–20, p< 0.001) was not statistically different to the risk of dying from severe dengue hemorrhagic fever (CFR 2.73%, RMR 19, 95% CI 17–22, p< 0.001) compared to individuals with dengue alone (non-severe dengue and no underlying comorbidity) (**Table 1**). The risk of dying was further significantly increased with the combination of severe dengue hemorrhagic fever and underlying comorbidities (CFR 15.33%, RMR 106, 95% CI 71–159, p< 0.001) compared to individuals with dengue alone (non-severe dengue and no underlying comorbidity). Furthermore, there was a 1.7 fold higher prevalence of severe dengue associated with comorbidities (8.4%, p< 0.001), compared to those without comorbidities (4.8%) (**Table 1**).

Thus, the presence of both comorbidities and severe dengue are cumulative risk factors for increased hospitalized dengue death rates. Comorbidities with highest dengue hospital death rates, regardless of dengue severity, were consistently renal disease, infectious disease, pulmonary disease and diabetes. However, in the presence of both severe dengue and underlying comorbidities, such as diabetes (CFR 25%), other non-dengue infectious diseases (CFR 20.83%), pulmonary disorders (CFR 20.59%), renal disease (CFR 15.38%), fatality rates were higher compared to individuals with non-severe dengue and no underlying comorbidities (**Table 1**).

To our knowledge, this is the largest retrospective cohort study of more than 300,000 hospitalized dengue cases (15,993 dengue hemorrhagic fever, 971 fatal cases) demonstrating

a high mortality in the presence of comorbidities in individuals 9–45 years of age in Brazil over an 8 year period. Our study demonstrated for the first time that risk of dengue death in the presence of comorbidities is similar to the risk of death from severe dengue and much higher with the combination of both comorbidities and severe dengue. The comorbidities contributing to increased death rates were consistently infectious diseases, pulmonary diseases, renal disease/failure and diabetes regardless of dengue severity.

Prior publications on the impact of underlying comorbidities on dengue related mortality are limited and inconsistent, in part related to the small number of deaths included in these analyses (Toledo et al. 2016). However, these reports suggest that underlying comorbidities can worsen dengue clinical outcomes.

Two large scale studies explored severe dengue as a risk factor for dengue mortality but did not specifically analyze the contribution of comorbidities. Both studies used the Brazilian Information System for Notifiable Diseases (SINAN) and gathered information on 281,159 and 105,459 dengue cases and 156 and 62 deaths, respectively (Campos et al. 2015; Pinto et al. 2016). Campos *et al.* reported that factors associated with dengue mortality included age >65 years and plasma leakage (Campos et al. 2015). Pinto *et al.* found that patients who died due to severe dengue had more hematuria, gastrointestinal bleeding, and thrombocytopenia than survivors (Pinto et al. 2016). In Brazil, there have been two further publications on a small series of patients. In a case-controlled study with 1345 patients in Brazil during 2003–2005 (n=170 dengue hemorrhagic fever cases), diabetes (OR 2.75; 95% CI 1.12–-6.73) was associated with dengue hemorrhagic fever (Figueiredo et al. 2010). In a later case-controlled study, in 1806 patients in Brazil during 2009–2012, hypertension (OR 1.6; 95% CI 1.1–2.1) and skin allergy (OR 1.8; 95% CI 1.1–3.2) increased the likelihood of progressing to dengue hemorrhagic fever but diabetes was not a confirmed risk factor in this report (Teixeira et al.

2015). A study of the 1981 dengue epidemic in Cuba found that chronic diseases such as bronchial asthma, diabetes mellitus and sickle cell anemia were more frequently observed in fatal dengue cases (Bravo et al. 1987). A number of other studies have also suggested that underlying comorbid conditions are common among dengue-related deaths, but these have generally been based on analyses that included very few deaths (typically, <15 deaths included in the analyses) (Guzman et al. 1999; Lahiri et al. 2008; Lee et al. 2005, 2008; Ong et al. 2007). The estimated CFR of 0.3% in all hospitalized dengue cases in our study was much lower than the 1.3% average reported to PAHO for Brazil during the same time period, but this may be due to differences in reporting of severe dengue, which may elevate the CFR in other studies. Furthermore, this may reflect the inherent differences in clinical case management practices and dengue diagnosis for dengue/severe dengue (Kalayanarooj 1999), or differences in circulating dengue virus serotypes which all co-circulate but varies unpredictably over time (Ocazionez et al. 2006; OhAinle et al. 2011). Although dengue diagnosis was based on a combination of clinical diagnosis and/or laboratory diagnosis, this reflects current clinical practice guidelines by WHO in countries where laboratory diagnosis may not be available. Although this study is descriptive, we have however conducted a more in depth analysis of the individual risk factors and determined that age, severe dengue and comorbidities are independent and cumulative risk factors for increased dengue mortality in Brazil and other countries in Latin America (submitted for publication). Despite the fact that we excluded all severe dengue symptoms and pathologies associated with severe dengue outcome, it is possible that there remains still some underlying bias whereby increased risk of death from comorbidities may be just a manifestation of severe dengue comorbidities. For example, we considered renal disease or failure as a comorbid condition, but acute renal failure may be a complication of severe dengue (Wiwanitkit 2005). However, overall the data on renal disease also included chronic renal failure and other underlying renal pathologies

which are not outcomes of severe dengue. Socioeconomic and healthcare factors may also play a role in dengue mortality; in Brazil, dengue mortality was shown to be associated with a number of socioeconomic and urbanization indicators (Paixao et al. 2015). Nonetheless, a major strength of our study is the large number of deaths assessed in our analysis, which encompasses reported cases across the whole of Brazil. Further, our study used the SIH/SUS reporting system which is unique in allowing the analysis of comorbidities in a detailed way.

In conclusion, the risk of dying from hospitalized dengue is 11 times higher in those with underlying common comorbidities. To our knowledge this is the largest retrospective analysis conducted in Brazil whereby comorbidities identified in a high proportion of dengue deaths were renal disease, infectious disease, pulmonary disease and diabetes. Ensuring access to dengue preventative measures including the recently available dengue vaccine (Dengvaxia®) in individuals with comorbidities may help achieve the WHO objective of 50% reduction in dengue-related mortality by 2020 (World Health Organization 2012).

Acknowledgements

This study was funded by Sanofi Pasteur including service provision of database consolidation, data mining and analysis by Ariana Pharmaceuticals. Editorial assistance with the preparation of the manuscript was provided by Richard Glover and Rebecca Hornby, inScience Communications, Springer Healthcare, Chester, UK. Funding for latter assistance was also provided by Sanofi Pasteur. The authors also thank Jean-Sébastien Persico for editorial assistance and manuscript coordination on behalf of Sanofi Pasteur.

Conflict of interest

AEM has no conflicts of interest. GW was partially funded by Sanofi Pasteur. CM, LC, EP-R, NB, and M-LT are employees of Sanofi Pasteur. DM, VR, and MG-K are employees of Ariana Pharmaceuticals who were contracted to undertake the analysis.

Authors' contribution

All authors were involved in the concept and design of the study. All authors contributed to the interpretation of the data and participated in the preparation of this manuscript, and approved the final manuscript for submission. All authors had access to the study data and are responsible for the veracity and completeness of the data reported.

References

Amancio FF, Heringer TP, de Oliveira Cda C, Fassy LB, de Carvalho FB, Oliveira DP, de Oliveira CD, Botoni FO, Magalhaes Fdo C, Lambertucci JR, Carneiro M 2015. Clinical Profiles and Factors Associated with Death in Adults with Dengue Admitted to Intensive Care Units, Minas Gerais, Brazil. *PLoS One*, 10, e0129046.

Ariana Pharmaceuticals SA. KEM® (Knowledge Extraction and Management) data mining platform.

Berthold MR, Cebron N, Dill F, Gabriel TK, Meinl T, Ohl P, Sieb C, Thiel K, Wiswedel B 2008. *KNIME: The Konstanz Information Miner.* Springer-Verlag Berlin-Heidelberg.

Bravo JR, Guzman MG, Kouri GP 1987. Why dengue haemorrhagic fever in Cuba? Individual risk factors for dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS). *Trans R Soc Trop Med Hyg*, 81, 816-820.

Campos KB, Amancio FF, de Araujo VE, Carneiro M 2015. Factors associated with death from dengue in the state of Minas Gerais, Brazil: historical cohort study. *Trop Med Int Health*, 20, 211-218.

Durand L, Genovez V, Araujo D 2017. Cost effectiveness of dengue vaccination in Brazil/ Custo-efetividade da vacinação contra dengue no Brasil. . *J Bras Econ Saude.* , 9, 12-29.

Fares RC, Souza KP, Anez G, Rios M 2015. Epidemiological Scenario of Dengue in Brazil. *Biomed Res Int*, 2015, 321873.

Figueiredo MA, Rodrigues LC, Barreto ML, Lima JW, Costa MC, Morato V, Blanton R, Vasconcelos PF, Nunes MR, Teixeira MG 2010. Allergies and diabetes as risk factors for dengue hemorrhagic fever: results of a case control study. *PLoS Negl Trop Dis*, 4, e699.

Guzman MG, Alvarez M, Rodriguez R, Rosario D, Vazquez S, Vald s L, Cabrera MV, Kouri G 1999. Fatal dengue hemorrhagic fever in Cuba, 1997. *Int J Infect Dis*, 3, 130-135.

Hotez PJ, Peiperl L 2015. Noncommunicable Diseases: A Globalization of Disparity? *PLoS Med*, 12, e1001859.

Kalayanarooj S 1999. Standardized clinical management: evidence of reduction of dengue haemorrhagic fever case-fatality rate in Thailand. *Dengue Bulletin*, 23, 10-17.

Lahiri M, Fisher D, Tambyah PA 2008. Dengue mortality: reassessing the risks in transition countries. *Trans R Soc Trop Med Hyg*, 102, 1011-1016.

Lee IK, Liu JW, Yang KD 2005. Clinical characteristics and risk factors for concurrent bacteremia in adults with dengue hemorrhagic fever. *Am J Trop Med Hyg*, 72, 221-226.

Lee IK, Liu JW, Yang KD 2008. Clinical and laboratory characteristics and risk factors for fatality in elderly patients with dengue hemorrhagic fever. *Am J Trop Med Hyg*, 79, 149-153.

Liquiere M, Sallantin J 1998. Structural Machine Learning With Galois Lattice and Graphs. ICML'98: 5th International Conference on Machine Learning. Madison, WI: 1998; 305-313.

Mehta P, Hotez PJ 2016. NTD and NCD Co-morbidities: The Example of Dengue Fever. *PLoS Negl Trop Dis*, 10, e0004619.

Ministério da Saúde. Sistema de Informações Hospitalares do SUS. http://sihd.datasus.gov.br/.

MS 2002. Ministério da Saúde. Fundação Nacional de Saúde. Ministério da Saúde. Programa Nacional de Controle da Dengue - PNCD, FUNASA, Brasília., 32.

Ocazionez RE, Cortes FM, Villar LA, Gomez SY 2006. Temporal distribution of dengue virus serotypes in Colombian endemic area and dengue incidence. Re-introduction of dengue-3 associated to mild febrile illness and primary infection. *Mem Inst Oswaldo Cruz*, 101, 725-731.

OhAinle M, Balmaseda A, Macalalad AR, Tellez Y, Zody MC, Saborio S, Nunez A, Lennon NJ, Birren BW, Gordon A, Henn MR, Harris E 2011. Dynamics of dengue disease severity determined by the interplay between viral genetics and serotype-specific immunity. *Sci Transl Med*, 3, 114ra128.

Ong A, Sandar M, Chen MI, Sin LY 2007. Fatal dengue hemorrhagic fever in adults during a dengue epidemic in Singapore. *Int J Infect Dis*, 11, 263-267.

PAHO 2017a. PAHO, Dengue: Annual Cases Reported of Dengue. . *http://www.paho.org/hq/index.php?option=com_topics&view=rdmore&cid=6290&Itemid=40734*.

Paixao ES, Costa Mda C, Rodrigues LC, Rasella D, Cardim LL, Brasileiro AC, Teixeira MG 2015. Trends and factors associated with dengue mortality and fatality in Brazil. *Rev Soc Bras Med Trop*, 48, 399-405.

Pan American Health Organization 2017b. Dengue: Data, Maps and Statistics. Data available from: http://www.paho.org/hq/index.php?option=com_topics&view=article&id=1&Itemid=40734 (Accessed 1 September 2017).

Pinto RC, Castro DB, Albuquerque BC, Sampaio Vde S, Passos RA, Costa CF, Sadahiro M, Braga JU 2016. Mortality Predictors in Patients with Severe Dengue in the State of Amazonas, Brazil. *PLoS One*, 11, e0161884.

Sarti E, L'Azou M, Mercado M, Kuri P, Siqueira JB, Jr., Solis E, Noriega F, Ochiai RL 2016. A comparative study on active and passive epidemiological surveillance for dengue in five countries of Latin America. *Int J Infect Dis*, 44, 44-49.

Shepard DS, Undurraga EA, Halasa YA, Stanaway JD 2016. The global economic burden of dengue: a systematic analysis. *Lancet Infect Dis*, 16, 935-941.

Team RDC 2011. *R: A Language and Environment for Statistical Computing*. . Vienna, Austria.

Teixeira MG, Paixao ES, Costa Mda C, Cunha RV, Pamplona L, Dias JP, Figueiredo CA, Figueiredo MA, Blanton R, Morato V, Barreto ML, Rodrigues LC 2015. Arterial hypertension and skin allergy are risk factors for progression from dengue to dengue hemorrhagic fever: a case control study. *PLoS Negl Trop Dis*, 9, e0003812.

Toledo J, George L, Martinez E, Lazaro A, Han WW, Coelho GE, Runge Ranzinger S, Horstick O 2016. Relevance of Non-communicable Comorbidities for the Development of the Severe Forms of Dengue: A Systematic Literature Review. *PLoS Negl Trop Dis*, 10, e0004284.

WHO 1997. Dengue haemorrhagic fever: diagnosis, treatment, prevention and control. 2nd edition. Geneva: World Health Organization.

WHO 2014. World Health Organization International Statistical Classification of Diseases and Related Health Problems 10th Revision. In.

Wiwanitkit V 2005. Acute renal failure in the fatal cases of dengue hemorrhagic fever, a summary in Thai death cases. *Ren Fail*, 27, 647.

World Health Organization 2012. Global strategy for dengue prevention and control, 2012–2020. Available at: http://apps.who.int/iris/bitstream/10665/75303/1/9789241504034_eng.pdf?ua=1 (Accessed 1 September 2017).

Table 1. Summary of comorbidities recorded in hospitalized dengue cases aged 9–45 years at admission (Brazilian Hospital Information System of the Unified Health System (SIH/SUS), 2008–2015).

Group	All dengue diagnoses (A90, A91)						Dengue fever diagnosis (A90)				Dengue hemorrhagic fever diagnosis (A91)				
	Cases	Female	Male	Deaths	CFR (%)	RMR[1] (95% CI)	Cases	Deaths	CFR (%)	RMR[2] (95% CI)	Cases	Deaths	CFR (%)	RMR[2] (95% CI)	Prevalence [3] (%)
All dengue cases	326380	173778	152602	971	0.30		310387	501	0.16		15993	470	2.94		4.9
with no 2nd diagnosis	320793	170726	150067	862	0.27	1	305311	440	0.14	1	15482	422	2.73	19 (17–22)***	4.8
with comorbidity	1629	871	758	50	3.07	11 (9–15)***	1492	29	1.94	13 (9–20)***	137	21	15.33	106 (71–159)***	8.4
infectious diseases‡	657	309	348	25	3.81	14 (10–21)***	609	15	2.46	17 (10–28)***	48	10	20.83	145 (83–253)***	7.3
pulmonary disorders	364	192	172	13	3.57	13 (8–23)***	330	6	1.82	13 (6–28)***	34	7	20.59	143 (73–278)***	9.3
urinary disorders	258	180	78	1	0.39	1 (0.2–10) ns	251	1	0.40	3 (0.4–20) ns	7				2.7
renal disease or failure	82	37	45	6	7.32	27 (13–59)***	69	4	5.80	40 (15–105)***	13	2	15.38	107 (30–383)***	15.9
HIV	70	33	37	1	1.43	5 (0.8–37) ns	59	1	1.69	12 (2–82) ns	11				15.7
Diabetes	61	37	24	2	3.28	12 (3–48)*	57	1	1.75	12 (2–85) ns	4	1	25.00	173 (32–950) **	6.6
heart failure	8	3	5	1			5	1			3				
Obesity	7	4	3				5				2				
Stroke	3	1	2	1			2				1	1			
ischemic heart disease	1		1				1								

RMR[1]: Relative Mortality Rate calculated relative to CFR for all dengue cases with no 2nd diagnosis
RMR[2]: Relative Mortality Rate calculated relative to CFR for dengue cases with A90 diagnosis and no 2nd diagnosis
Significance (Fisher): *** ($p < 0.001$); ** ($p < 0.01$); * ($p < 0.05$); ns ($p > 0.05$)
[3] Prevalence: percentage of dengue cases with dengue hemorrhagic fever diagnosis (A91)

ǂInfectious diseases: dengue cases with a secondary (comorbidity) diagnosis of "infectious diseases" (excluding dengue) recorded; i.e. patient had dengue and another infectious disease (ICD10 A code).

Supplementary material

Table S1. ICD10 code definitions for comorbidity groups

Comorbidity	ICD10 Code	Description
Diabetes	E10	Insulin-dependent diabetes mellitus
	E11	Non-insulin-dependent diabetes mellitus
	E13	Other specified diabetes mellitus
	E14	Unspecified diabetes mellitus
HIV	B20	Human immunodeficiency virus [HIV] disease resulting in infectious and parasitic diseases
	B22	Human immunodeficiency virus [HIV] disease resulting in other specified diseases
	B23	Human immunodeficiency virus [HIV] disease resulting in other conditions
	B24	Unspecified human immunodeficiency virus [HIV] disease
Heart failure	I50	Heart failure
Ischemic heart disease	I20	Angina pectoris
	I21	Acute myocardial infarction
	I24	Other acute ischemic heart diseases
	I25	Chronic ischemic heart disease
Obesity	E66	Obesity
Pulmonary disorders	J12	Viral pneumonia, not elsewhere classified
	J15	Bacterial pneumonia, not elsewhere classified
	J18	Pneumonia, organism unspecified
	J21	Acute bronchiolitis
	J40	Bronchitis, not specified as acute or chronic
	J44	Other chronic obstructive pulmonary disease
	J45	Asthma
	J90	Pleural effusion, not elsewhere classified
	J96	Respiratory failure, not elsewhere classified
Renal disease or failure	N10	Acute tubulo-interstitial nephritis
	N11	Chronic tubulo-interstitial nephritis
	N12	Tubulo-interstitial nephritis, not specified as acute or

Comorbidity	ICD10 Code	Description
		chronic
	N13	Obstructive and reflux uropathy
	N18	Chronic kidney disease
	N17	Acute renal failure
	N19	Unspecified kidney failure
Stroke	I64	Stroke, not specified as hemorrhage or infarction
Urinary disorders	N39	Other disorders of urinary system
Infectious disease	A00-A99	Infectious diseases (excluding dengue A90/91)