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Prevalence and clinical outcomes of myocarditis and pericarditis in 718,365 COVID-19 patients

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Manuscript wordcount 2,268

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Abstract

Background

COVID-19 has a wide spectrum of cardiovascular sequelae including myocarditis and pericarditis; however, the prevalence and clinical impact is unclear. We investigated the prevalence of new-onset myocarditis/pericarditis and associated adverse cardiovascular events in patients with COVID-19.

Methods and Results

A retrospective cohort study was conducted using electronic medical records from a global federated health research network. Patients were included based on a diagnosis of COVID-19 and new-onset myocarditis or pericarditis. Patients with COVID-19 and myocarditis/pericarditis were 1:1 propensity score matched for age, sex, race and co-morbidities to patients with COVID-19 but without myocarditis/pericarditis. The outcomes of interest were 6-month all-cause mortality, hospitalisation, cardiac arrest, incident heart failure, incident atrial fibrillation, and acute myocardial infarction, comparing patients with and without myocarditis/pericarditis.

Of 718,365 patients with COVID-19, 35,820 (5.0%) developed new onset myocarditis and 10,706 (1.5%) developed new onset pericarditis. Six-month all-cause mortality was 3.9% (n=702) in patients with myocarditis and 2.9% (n=523) in matched controls (*P*<0.0001), odds ratio 1.36 (95% confidence interval (CI): 1.21-1.53). Six-month all-cause mortality was 15.5% (n=816) for pericarditis and 6.7% (n=356) in matched controls (P<0.0001), odds ratio 2.55 (95% CI: 2.24-2.91). Receiving critical care was associated with significantly higher odds of mortality for patients with myocarditis and pericarditis. Patients with pericarditis seemed to associate with more new-onset cardiovascular sequelae than those with myocarditis. This finding was consistent when looking at pre-COVID-19 data with pneumonia patients.

Conclusions

Patients with COVID-19 who present with myocarditis/pericarditis associate with increased odds of major adverse events and new-onset cardiovascular sequelae.

Keywords

COVID-19; Cardiovascular sequelae; Myocarditis; Pericarditis; MACE

Declarations

Funding

No specific funding was received for this study. TriNetX LLC., funded the acquisition of the data.

Conflicts of interest/Competing interests

Benjamin JR Buckley has received funding from Bristol-Myers Squibb (BMS)/Pfizer. Stephanie L Harrison has received funding from BMS. Elnara Fazio-Eynullayeva and Paula Underhill are employees of TriNetX LLC. Deirdre A Lane has received investigator-initiated educational grants from BMS, has been a speaker for Boehringer Ingeheim, and BMS/Pfizer and has consulted for BMS, Boehringer Ingelheim, and Daiichi-Sankyo. Gregory YH Lip: consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon and Daiichi-Sankyo and speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received personally.

Availability of data and material

To gain access to the data in the TriNetX research network, a request can be made to TriNetX (https://live.trinetx.com), but costs may be incurred, a data sharing agreement would be necessary, and no patient identifiable information can be obtained.

Code availability

Not applicable

Ethics approval

As a federated network, research studies using the TriNetX network do not require ethical approval or patient informed consent as no patient identifiable information is received.

Consent to participate

Not applicable

Consent for publication

Not applicable

Introduction

Myocarditis and pericarditis are non-ischaemic inflammatory diseases of the myocardium and pericardium, respectively.(1,2) The clinical presentation of these two conditions are highly variable and may be proceeded by coryzal symptoms or non-specific features of general malaise, fatigue, or diarrhoea. At the other extreme, cardiac inflammation may stimulate myocardial infarction, symptomatic arrhythmias, heart failure, cardiogenic shock, or sudden cardiac death.(3) Although the aetiology of myocarditis and pericarditis is heterogenous, infection is the most common cause,(1) with viral pathogens the most commonly implicated in the developed world.(4)

The hallmark of COVID-19 is respiratory involvement, ranging from mild upper respiratory symptoms to acute respiratory distress syndrome.(5) However, severe COVID-19 has been implicated in multi-organ involvement, with several observational case series showing a significant proportion of cardiac involvement among hospitalized patients.(6-8) Moreover, cardiac injury seems to be significantly correlated with increased in-hospital mortality in COVID-19 patients.(7) COVID-19 has a wide spectrum of cardiovascular sequelae, including acute-onset heart failure, arrhythmias, acute coronary syndrome, myocarditis, and cardiac arrest. A growing body of evidence has described cardiac involvement in COVID-19, including myocarditis,(9,10), pericarditis,(11) or more generally, increased biomarkers of cardiac injury,(12) all of which may associate with poor prognosis.(13,14)

Despite recent case reports, the prevalence and clinical impact of new-onset presentation of myocarditis and pericarditis in adults with COVID-19 is unclear. Therefore, using a global federated health research network, the aim of the present study was to investigate the prevalence and associated adverse events and cardiovascular sequelae in patients with COVID-19 who also present with new-onset myocarditis/pericarditis.

Methods

Study Design and Participants

A retrospective observational study was conducted within TriNetX, a global federated health research network with access to electronic medical records (EMRs) from participating healthcare organisations including academic medical centres, specialty physician practices, and community hospitals, predominantly in the United States. The TriNetX network was searched on August 19, 2021 for patients with COVID-19 aged 18-90 years identified in EMRs between January 20, 2020 and June 1, 2020. In addition, a pre-COVID-19 cohort was included (between January 20, 2019 and June 1, 2019) presenting patients with an EMR of pneumonia to validate the prevalence and associated outcomes of myocarditis/pericarditis observed in the COVID-19 cohorts. Reporting of this study conforms to broad EQUATOR guidelines(15) and the more specific Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.(16)

Patients with COVID-19 were identified following criteria provided by TriNetX based on Centers for Disease Control and Prevention (CDC) coding guidelines (17). Patients were included if they had one or more of the following International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes in patient EMRs: U07.1 COVID-19; B97.29 Other coronavirus as the cause of diseases classified elsewhere; B34.2 Coronavirus infection, unspecified; or a positive test result identified with COVID-19 specific laboratory Logical Observation Identifiers Names and Codes (LOINCs). Myocarditis was identified with the following ICD-10-CM codes in patient EMRs: I40, Acute Myocarditis; I41, Myocarditis in diseases classified elsewhere; I51.4 Myocarditis, unspecified; B97.8 Other viral agents as the cause of diseases classified elsewhere; or B89, Unspecified parasitic disease. Pericarditis was identified with the following ICD-10-CM codes in patient EMRs: I30, Acute pericarditis; I31, Other diseases of the pericardium; I32, Pericarditis in disease classified elsewhere. Pneumonia (used to validate the COVID-19 analyses) was identified by ICD-10-CM code, J18.

The TriNetX platform only uses aggregated counts and statistical summaries of de-identified information. No Protected Health Information or personal data is made available to users of the platform. Thus, research studies using the TriNetX research network do not require ethical

approval as no identifiable patient data is received. TriNetX database performs extensive internal data quality assessments with every refresh based on conformance, completeness, and plausibility.(18) This includes the evaluation of clinical correctness and agreements of network insights with external information.

Data Collection

The TriNetX network was searched on August 19, 2020 and an anonymised dataset of patients was analysed within the online database. The COVID-19 cohort, both with and without myocarditis/pericarditis, were aged ≥18 years with a diagnosis between January 20, 2020 (date COVID-19 first confirmed in the US)(19) and June 1, 2020 (allowing for 6-month follow-up). At the time of the search, 53 participating healthcare organisations had data available for patients who met the study inclusion criteria.

Statistical Analysis

All statistical analyses were completed within the TriNetX online platform. Baseline characteristics were compared using chi-squared tests for categorical variables and independent-sample t-tests for continuous variables. Propensity score matching (PSM) was used to control for differences in the cohorts and/or known risk factors for cardiovascular disease and all-cause mortality. PSM was therefore used to match patients with COVID-19 and myocarditis/pericarditis to patients with COVID-19 without myocarditis/pericarditis. PSM was also conducted for the pneumonia cohort analyses with and without myocarditis/pericarditis. Patients were 1:1 PSM using logistic regression for age, sex, race, hypertensive diseases, ischaemic heart diseases, heart failure, cerebrovascular diseases, diabetes mellitus, chronic kidney disease, diseases of the respiratory system, diseases of the digestive system, and diseases of the nervous system. These variables were chosen because they are established risk factors for cardiovascular disease and/or mortality or were significantly different between the two cohorts. The TriNetX platform uses 'greedy nearest-neighbour matching' with a caliper of 0.1 pooled standard deviations. Following PSM, logistic regressions produced odds ratios with 95% confidence intervals (CIs) for 6-month incidence of all-cause mortality, hospitalisation, cardiac arrest, incident heart failure, incident atrial fibrillation (AF), and acute myocardial infarction, comparing patients with/without myocarditis and pericarditis. Statistical significance was set at $P<0.05$.

Results

Patient characteristics

The COVID-19 cohort used in this study was distributed between the four large Census Bureau designated regions of the US as follows: 17% in the Northeast, 19% in the Midwest, 45% in the South, and 19% in the West. Of 718,365 patients with COVID-19, 35,820 (5.0%) developed new-onset myocarditis and 10,706 (1.5%) developed new-onset pericarditis. Compared to propensity matched controls, patients who developed myocarditis/pericarditis had higher proportions of comorbidities. Although not all variables were statistically non-significant, following PSM, the myocarditis (**Supplementary Table 1**) and pericarditis (**Supplementary Table 2**) cohorts were deemed well-matched.

Myocarditis and COVID-19

Following PSM, six-month all-cause mortality was 3.9% (n=702) in patients with COVID-19 who presented with myocarditis and 2.9% (n=523) in the matched controls without myocarditis (*P*<0.0001), odds ratio 1.36 (95% CI: 1.21-1.53). Associated odds of rehospitalisation (odds ratio 1.90 (95% CI 1.80-2.01) and acute myocardial infarction (odds ratio 1.37 (95% CI 1.17-1.61) were also higher in the myocarditis cohort compared to controls. Associated odds of cardiac arrest, incident heart failure, and incident AF, were not significantly different between the myocarditis cohort and controls. Among subgroups, mortality was higher in all except those aged <45 years and those not hospitalised following COVID-19 (**Table 1**).

Pericarditis and COVID-19

Following PSM, six-month all-cause mortality was 15.5% (n=816) in patients with COVID-19 who presented with new-onset pericarditis and 6.7% (n=356) in the matched controls without pericarditis (P<0.0001), odds ratio 2.55 (95% CI: 2.24-2.91). Associated odds of rehospitalisation, cardiac arrest, incident heart failure, incident AF, and acute myocardial infarction were also significantly higher in the pericarditis cohort compared to controls. Mortality was higher among all subgroups (**Table 2**).

Pneumonia and myocarditis/pericarditis (Pre-COVID-19 analyses)

Of the total pneumonia cases (n=128,939), 3.1% (n=4,012) developed myocarditis and 1.9% (n=2,497) developed pericarditis. Myocarditis was associated with significantly higher odds of rehospitalisation compared to controls. Pericarditis was associated with significantly higher odds for mortality, rehospitalisation, cardiac arrest, heart failure, AF, and myocardial infarction. The complete prevalence and outcome data for the pneumonia cohort is presented in **Supplementary Table 3**.

Discussion

Collectively, this retrospective analysis represents the largest follow-up data set of its kind for patients with COVID-19 and presentation of new-onset myocarditis or pericarditis. The findings of the present study suggest that myocarditis and pericarditis in patients with COVID-19 associates with significantly increased odds of all-cause mortality, rehospitalisation, and acute myocardial infarction. Associated odds of cardiac arrest, incident heart failure, and incident AF, were higher in patients with pericarditis compared to matched controls. In contrast, associated odds of cardiac arrest, incident heart failure, and incident AF were not higher in patients with myocarditis compared to matched controls. Therefore, although new-onset myocarditis was more prevalent (5.0%) than pericarditis (1.5%) in patients with COVID-19, the latter seems to be associated with more substantial adverse events and cardiovascular sequelae.

Previous work has demonstrated that in 222 non-COVID-19, biopsy-proven, viral myocarditis cases, the rate of mortality was 19.2% in 4.7 years of follow-up.(20) In a nationwide Danish registry of 8,077 patients with pericarditis, the absolute 1-year mortality was 2.9% compared to 0.8% in matched controls without pericarditis.(21) In the present study, results demonstrate the associated odds of adverse events and cardiovascular sequelae between COVID-19 patients with myocarditis/pericarditis and patients with COVID-19 only. Odds of mortality were 1.90 (95% CI 1.80-2.01) and 2.55 (95% CI: 2.24-2.91) in patients with myocarditis and pericarditis, respectively. Although this has not been previously investigated, these findings are complimentary to that of Shi *et al* who demonstrated that cardiac injury was common (19.7%) among 416 hospitalised patients with COVID-19 in Wuhan, China.(7)

Moreover, patients with cardiac injury had higher mortality (51.2%) than those without cardiac injury (4.5%; P < .001), and those who received intensive care, were more likely to have cardiac injury.

Although we did not investigate cardiac injury per se, we also found an increasing magnitude of the odds of mortality associated with COVID-19 severity, measured by proxy from hospitalisation records. Indeed, data suggested a dose-response, with 68% (1.40-2.00) and 195% (2.19-3.97) higher odds of all-cause mortality in COVID-19 patients with myocarditis who were either hospitalised or received critical care, respectively. Moreover, there was no increase in the odds of mortality in COVID-19 patients with myocarditis who were not hospitalised with COVID-19 initially. Similarly, for COVID-19 patients with pericarditis, there were increasing odds of all-cause mortality in patients who were not hospitalised, hospitalised, and received critical care following a COVID-19 diagnosis. Thus, the clinical importance of new-onset myocarditis/pericarditis in patients with COVID-19 seems to be dependent on the severity of initial viral infection.

In a cohort of German patients recently recovered from COVID-19, cardiac magnetic resonance revealed ongoing myocardial inflammation in 60 patients (60%), independent of pre-existing conditions, severity, overall course of the acute illness, and time from the original diagnosis.(6) This aligns with previous non-COVID-19 research that demonstrated clinical presentation with congestive heart failure, ventricular tachycardia/ventricular fibrillation, or AF/atrial flutter did not predict survival in patients with myocarditis.(22) In contrast and in the present study, patients who presented with new-onset myocarditis/pericarditis had higher proportions of comorbidities including cardiovascular, metabolic, nervous, and digestive conditions. This is in keeping with a previous study whereby patients with pre-existing cardiovascular diseases seemed to be more susceptible to COVID-19–induced heart injury. Specifically, 30% and 60% of patients with cardiac injury had a history of coronary heart disease and hypertension, respectively; which were significantly more prevalent than in those without cardiac injury.(7)

In a single case of COVID-19 in a young child, it was proposed that there was a direct effect of the SARS-CoV-2 infection on cardiac tissue, which in this case, was a major contributor to the

presentation of new-onset myocarditis and heart failure.(23) This case, among others(24,25) provides evidence that COVID-19 may be a multisystem inflammatory syndrome(26) and as in the present study, its cardiovascular sequelae present a significant risk to health. It has been proposed that the pathophysiology of viral myocarditis is a combination of direct cell injury and T-lymphocyte–mediated cytotoxicity, which can be augmented by the cytokine storm syndrome.(27) Mechanisms for COVID-19 associated myocarditis/pericarditis may therefore be similar, given that myocardial localization of COVID-19 has been reported in a case study of a 69-year-old who received endomyocardial biopsy.(28)

Limitations

A number of limitations are noteworthy. First, the data were collected from health care organization EMR databases and some health conditions may be underreported. Indeed, recording of ICD codes in administrative datasets may vary by factors such as age, number of comorbidities, severity of illness, length of hospitalisation, and whether in-hospital death occurred.(29) Specifically, the method of diagnosis of myocarditis/pericarditis from EMRs is unknown. However, we have investigated the prevalence and clinical outcomes of myocarditis and pericarditis following a pneumonia diagnosis in January-June 2019 (i.e., pre-COVID-19), in order to verify associations with cardiovascular outcomes in the COVID-19 cohort. Findings revealed that of the total pneumonia cases (n=128,939), 3.1% (n=4,012) developed myocarditis and 1.9% (n=2,497) developed pericarditis (lower, albeit not dissimilar from prevalence in the COVID-19 cohort). In the pneumonia cohort, myocarditis was associated with significantly higher odds of rehospitalisation only, whereas pericarditis associated with significantly higher odds for all outcomes (mortality, hospitalisation, cardiac arrest, heart failure, atrial fibrillation, and myocardial infarction; **Supplementary Table 3**). This is largely aligned with the higher odds of cardiovascular outcomes observed with pericarditis compared to myocarditis in the COVID-19 cohort, presented in this paper. We could also not determine the influence of attending different healthcare organizations due to data privacy restrictions. In addition, outcomes which occurred outside of the TriNetX network are not well captured. Second, the data were from multiple healthcare organizations in the United States but may not be representative of the wider population, thus the generalisability of the results beyond this cohort is unclear. Third, longer follow-up time

periods (beyond 6-months) would be interesting, particularly for mortality and cardiovascular disease outcomes. Fourth, immortal time bias needs to be considered when interpreting rates of myocarditis and pericarditis in patients with COVID-19. It is possible that the rates reported in this study are an underrepresentation of the true prevalence. Further, our results should not be interpreted as causal i.e., it can only be interpreted that new-onset myocarditis/pericarditis was associated with higher mortality rates seen in the present study; we do not know if myocarditis/pericarditis are determinants, contributors, or markers of effect. Indeed, residual confounding may have impacted our results, including lifestyle factors, socioeconomic status, and other health markers/conditions, which were not available from EMRs. Subsequent prospective work is needed to further investigate the cardiac involvement of COVID-19, especially in patients presenting with severe cases.

Conclusion

Findings from the present study suggest that COVID-19 patients who present with new-onset myocarditis/pericarditis are associated with significantly higher odds of all-cause mortality, relative to patients with COVID-19 only. Further, the severity of COVID-19 seems to be associated with more severe outcomes among patients with myocarditis and pericarditis. Finally, although myocarditis was more prevalent, pericarditis seemed to be associated with higher odds of mortality and new-onset cardiovascular sequelae (a finding that we have confirmed in pre-COVID-19 pneumonia analyses). Therefore, the targeting of early intervention and monitoring for patients with new-onset myocarditis/pericarditis following a COVID-19 diagnosis should be considered for populations with pre-existing cardiovascular disease and risk factors.

REFERENCES

1. Caforio ALP, Pankuweit S, Arbustini E et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. European Heart Journal 2013;34:2636-2648.
2. Imazio M, Gaita F, LeWinter M. Evaluation and Treatment of Pericarditis: A Systematic Review. JAMA 2015;314:1498-1506.
3. Eckart Robert E, Shry Eric A, Burke Allen P et al. Sudden Death in Young Adults. Journal of the American College of Cardiology 2011;58:1254-1261.
4. Breinholt JP, Moulik M, Dreyer WJ et al. Viral epidemiologic shift in inflammatory heart disease: The increasing involvement of parvovirus B19 in the myocardium of pediatric cardiac transplant patients. The Journal of Heart and Lung Transplantation 2010;29:739-746.
5. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020;323:1239-1242.
6. Puntmann VO, Carerj ML, Wieters I et al. Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19). JAMA Cardiology 2020;5:1265-1273.
7. Shi S, Qin M, Shen B et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol 2020;5:802-810.
8. Xu Z, Shi L, Wang Y et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. The Lancet Respiratory Medicine 2020;8:420-422.
9. Kim I-C, Kim JY, Kim HA, Han S. COVID-19-related myocarditis in a 21-year-old female patient. European Heart Journal 2020;41:1859-1859.
10. Inciardi RM, Lupi L, Zaccone G et al. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). JAMA Cardiology 2020;5:819-824.
11. Kumar R, Kumar J, Daly C, Edroos SA. Acute pericarditis as a primary presentation of COVID-19. BMJ Case Reports 2020;13:e237617.
12. Bhandari SS, Yeo J, Kotecha D, McCann GP. Fulminant micro and macroangiopathic sequalae in a patient with COVID-19. European Heart Journal - Case Reports 2020.
13. Pirzada A, Mokhtar AT, Moeller AD. COVID-19 and Myocarditis: What Do We Know So Far? CJC Open 2020;2:278-285.
14. Siripanthong B, Nazarian S, Muser D et al. Recognizing COVID-19–related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. Heart Rhythm 2020;17:1463-1471.
15. Simera I, Moher D, Hoey J, Schulz KF, Altman DG. A catalogue of reporting guidelines for health research. Eur J Clin Invest 2010;40:35-53.
16. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Journal of clinical epidemiology 2008;61:344-9.
17. Centers for Disease Control and Prevention. ICD-10-CM Official Coding Guidelines - Supplement Coding encounters related to COVID-19 Coronavirus Outbreak. 2020.

18. Kahn MG, Callahan TJ, Barnard J et al. A Harmonized Data Quality Assessment Terminology and Framework for the Secondary Use of Electronic Health Record Data. EGEMS (Wash DC) 2016;4:1244.
19. Holshue ML, DeBolt C, Lindquist S et al. First Case of 2019 Novel Coronavirus in the United States. The New England journal of medicine 2020;382:929-936.
20. Grün S, Schumm J, Greulich S et al. Long-Term Follow-Up of Biopsy-Proven Viral Myocarditis. Journal of the American College of Cardiology 2012;59:1604-1615.
21. Sigvardt FL, Hansen ML, Kristensen SL et al. Increased 1-year mortality among patients discharged following hospitalization for pericarditis - a nationwide cohort study. European Heart Journal 2019;40.
22. Magnani JW, Danik HJ, Dec GW, Jr., DiSalvo TG. Survival in biopsy-proven myocarditis: a long-term retrospective analysis of the histopathologic, clinical, and hemodynamic predictors. Am Heart J 2006;151:463-70.
23. Dolhnikoff M, Ferreira Ferranti J, de Almeida Monteiro RA et al. SARS-CoV-2 in cardiac tissue of a child with COVID-19-related multisystem inflammatory syndrome. The Lancet Child & Adolescent Health 2020;4:790-794.
24. Clerkin KJ, Fried JA, Raikhelkar J et al. COVID-19 and Cardiovascular Disease. Circulation 2020;141:1648-1655.
25. Doyen D, Moceri P, Ducreux D, Dellamonica J. Myocarditis in a patient with COVID-19: a cause of raised troponin and ECG changes. The Lancet 2020;395:1516.
26. Roberts CM, Levi M, McKee M, Schilling R, Lim WS, Grocott MPW. COVID-19: a complex multisystem disorder. Br J Anaesth 2020;125:238-242.
27. Esfandiarei M, McManus BM. Molecular Biology and Pathogenesis of Viral Myocarditis. Annual Review of Pathology: Mechanisms of Disease 2008;3:127-155.
28. Tavazzi G, Pellegrini C, Maurelli M et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. European Journal of Heart Failure 2020;22:911-915.
29. Chong WF, Ding YY, Heng BH. A comparison of comorbidities obtained from hospital administrative data and medical charts in older patients with pneumonia. BMC Health Serv Res 2011;11:105-105.