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1. ABSTRACT

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: *Not applicable*			
Name of active ingredient: *Not applicable*			
Report date: 12 Nov 2022	**Study number:** 1245-0203	**Version/Revision:** 1.0	**Version/Revision date:** 12 Nov 2022
Title of study:	Clinical characteristics and disease burden of patients with diabetes mellitus combined with cardiovascular or chronic kidney disease based on regional medical database in Tianjin China		
Keywords:	Clinical characteristics, disease burden, diabetes, regional medical database in China		
Rationale and background:	Diabetes has been a major public health concern all over the world. According to the data from the International Diabetes Federation (IDF) Diabetes Atlas 2017 [R18-1272], there are now around 425 million adults aged 20–79 worldwide living with diabetes. In China, the prevalence of diabetes among adults was 10.9%, representing an estimated 114.4 million Chinese adults with diabetes. The mortality among patient with diabetes was high, which estimated that 4 million adults died from diabetes worldwide in 2017 [R18-1272]. And diabetes has become a worrying burden upon the world's healthcare system recently [R18-1272, R22-3907, R22-1176]. The heavy disease burden is mainly due to diabetic complications. Diabetes is a major risk factor for cardiovascular disease (CVD) [R09-4241, R22-3908] and chronic kidney disease (CKD) [R18-1272, R09-4241]. The prevalence of CVD and CKD among patients with diabetes is high. Studies suggested that diabetic kidney disease developed in up to 50% of diabetic patients at 20		

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	years, with 15% having progressed to ESRD by this time [R22-3909]. Compared to non-diabetes, the risk of CVD and CKD increased in patients with diabetes [R18-1272]. A meta-analysis including 102 studies showed that patients with diabetes had an overall twice higher risk of coronary heart disease (CHD) than patients without diabetes [R12-2030]. Except for the risk of CVD and CKD, clinical characteristics and treatment patterns may also differ among patients with or without diabetes. Studies showed diabetic patients may have a greater burden of other risk factors than nondiabetics, such as hypertension, hyperlipidemia, and obesity [R12-3889]. Moreover, the effect of treatment on patients with or without diabetes may differ, thus the treatment patterns may be different. However, the characteristic profile of Chinese diabetic patients who have CVD, CKD or are at high risk of CVD remains unclear thus in-depth investigation is in urgent need. Several studies have shown that diabetes patients often suffer from multiple comorbidities, including the CVD and clearly described the characteristics and treatment patterns of such patients. However, patient characteristics and treatment patterns may differ across regions and hospitals. Lack of adequate understanding of such information may result in suboptimal management of patients and policy decisions. This is particularly true in China. In current China, however, the information regarding diabetes or non-diabetes patients who also had other comorbid conditions (e.g., established CVD, CKD or at high risk of such problem) is limited; the patient characteristics, treatment patterns and economic burden may not be fully understood. Tianjin regional database, which cover individual-level health information, is a valuable data source for clinical studies. Therefore, based on Tianjin regional database, we described the demographic, clinical characteristics, treatment, and economic burden of disease of Chinese diabetic/non-diabetic patients with/without established CVD, CKD, or at high CV risk including hypertension and hyperlipidemia. And we believe that the resulting findings will provide relevant evidence to achieve better healthcare for diabetes patients with established or at high risk of CVD or CKD.

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Research question and objectives:	The study aims to investigate the clinical characteristics, treatment, and economic burden of disease of Chinese diabetic/non-diabetic patients with/without established cardiovascular disease, chronic kidney disease, or at high cardiovascular risk.
Study design:	Non-interventional cross-sectional study based on regional existing medical database.
Setting:	All diabetic/non-diabetic patients with/without established cardiovascular disease, or chronic kidney disease, or at high cardiovascular risk were included in Tianjin regional database from 01/01/2015 to 31/12/2019. Patients with non-Chinese nationalities, abnormal birthdate or duplicated storage (records with same inpatient code) were excluded from this study. Patients without diabetes were selected randomly for comparison with diabetic patients.
Subjects and study size, including dropouts:	This study was conducted based on the Tianjin regional database from 01/01/2015 to 31/12/2019, there are 1,233,162 patients included into this study totally. Of those, 576,973 were diabetic patients with comorbidities, 253,012 were diabetic patients without comorbidities, 198,099 were non-diabetic patients with comorbidities, and 205,078 were non-diabetic patients without comorbidities.
Variables and data sources:	Variables include demographic characteristics, comorbidities, treatment pattern and economic burden. Data source is Tianjin regional database from 01/01/2015 to 31/12/2019, it comprises of EMR system data from 62 secondary and tertiary hospitals.
Results:	The proportions of patients with established CVD, CKD and at high cardiovascular risk among diabetic patients were high. In the year of 2019, the proportions of diabetic patients with established CVD, CKD and at high cardiovascular risk accounted for 54.0%, 10.8% and 57.0% respectively. In comparison, for non-diabetic patients with established CVD, CKD and at high cardiovascular risk accounted for 34.2%, 3.2% and 39.6% respectively. Diabetic patients with comorbidities were older . In 2015, the mean age among diabetic patients with and without comorbidities was 64 and 49 years respectively.. Department of internal medicine was visited mostly by diabetic patients. In 2015, 61.4% outpatients and 69.5% inpatients visited or discharged from department of internal

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	medicine, the proportion was 60.9% and 65.4% in 2019 for diabetic patients with comorbidities. Diabetic patients with comorbidities had longer length of stay (9 [6, 14] days vs. 6 [4, 10] days), higher proportion of re-hospitalization (46.8% vs. 15.2%), higher hospitalization cost (RMB 28,218.0 vs. RMB 11,330.0) than those without comorbidities. The total hospitalization cost increased from 2015 to 2019, while the outpatients cost decreased for all patients except non-diabetic patients without comorbidities.
Discussion:	Our findings indicate that diabetes is an important disease burden in China. For instance, among diabetic patients, 54.0% patients were diagnosed as CVD. The proportion of CVD in our study was higher than previously published studies in China because of the broader definition of CVD and different characteristics of included study population [R22-2341, R22-3904, R19-2698]. The high proportion of patients at high cardiovascular risks was similar to other studies, which suggested a comprehensive management of hypertension and hyperlipidemia in patients with diabetes is needed [R22-2341, R22-3905, R22-3925, P18-03979, R22-3906, R10-5437, P22-08928, P18-00092]. Diabetic patients with comorbidities were more likely to be admitted to the department of cardiology [R22-3904, R22-3910], while diabetic patients without comorbidities were more likely to be admitted to the department of obstetrics and gynecology, and the department of surgery. Our findings suggest that the proportion of gestational diabetes mellitus (GDM) was high among diabetic patients without comorbidities [R22-3911]. Compared to patients without comorbidities, diabetic patients with comorbidities were more likely to be prescribed with anti-diabetes drugs, antiplatelets and statins [P22-08928, P18-00092, R22-3912, R22-3916]. Insulin was more likely to be prescribed for inpatients. This may be because inpatients were generally in a worse health condition, and patients with high level of HbA1c or severe comorbidities were more likely to be treated with insulin [R22-3913, R22-3914]. Our study showed that the proportion of patients with established CVD, CKD and at high cardiovascular risk among diabetic patients were high. The clinical characteristics and treatment pattern differed between diabetic patient with and without comorbidities. The total medical cost was higher among diabetic patients with comorbidities

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	than those without. Diabetes poses a growing economic burden in China, and comorbidities is one of important problems that result in increased disease burden. Efforts should be made to fill the gaps in prevention and management of diabetes and comorbidities. Early screening and patient management, as well as investing in education are needed to improve the prognosis of patients with diabetes. However, our study had several limitations. First, study participants were identified according to ICD code, which may cause some misclassification. Secondly, our findings were exclusively based on data from secondary and tertiary hospitals in Tianjin. The findings of this study may not be generalizable to other settings. Moreover, information regarding clinical care in other hospitals were not collected, which may lead to information bias. Thirdly, non-diabetic patients without comorbidities were randomly selected and matched with diabetic patients with comorbidities according to their birthdate and sex, which may not represent all non-diabetic patients without comorbidities.
Marketing Authorisation Holder(s):	Not applicable
Names and affiliations of principal investigators:	[redacted] [redacted] China

2. LIST OF ABBREVIATIONS

ACEI	Angiotensin Converting Enzyme Inhibitors
AE	Adverse Event
ARB	Angiotensin Receptor Blocker
AUC	Area Under the Curve
CCB	Calcium Channel Blockers
CHD	Coronary Heart Disease
CI	Confidence Interval
CML	Local Clinical Monitor
CRA	Clinical Research Associate
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
CTMF	Clinical Trial Master File