Measures to improve drug compliance of young women with acute myocardial infarction: According to the influncing factors

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Abstract: Acute myocardial infarction (AMI) accounts for approximately 16% of global mortality[1]. Young women, as a non-traditional high-risk group, suffers from AMI in a different way. In this review, we aim to study how to improve drug compliance in this subgroup of young female patients with acute myocardial infarction. We analyzed this matter from five perspectives: patient factors, socioeconomic factors, medical system factors, treatment factors, and technology factors. Educational level, as a patient factor, play an essential role. Results showed that patient's drug compliance is positively associated with level of education, yet health education will effectively close the gap. As for socio-economic factors, drug and follow-up visit to the hospital serve as burdens for those in poverty, furthermore, support from families and the society also play an integral role in improving prognosis. Medical system composes of education and the accessability of medical resources for patients. Nowadays, doctor-patient relationship in China is far from optimistic, therefore practical educational method should be put forward. As for medical resources scarcity, communitybased clinics ought to exercise their responsibility. Treatment factors mainly consists of side effect and usage of the prescripted drugs. Patients' fear of existing or non-existing side effect greatly affect compliance, and could be solved by education and better drug development. Polypill might be the answer for the complexity of treatment. In addition, we consider the feasibility of adopting new technologies among young female patients, and propose the use of smartphones for medication alerts to improve drug compliance among young female patients, etc.

1. Introduction

Acute myocardial infarction (AMI) attacks approximately three million people worldwide each year. AMI can be segmented into non-ST-segment elevation MI (NSTEMI) and ST-segment elevation MI (STEMI) [2]. Compared with men, female patients have higher rates of bleeding, stroke, readmission, and mortality after acute myocardial infarction. Such sex difference can be attributed to the pathophysiology aspect, particularly the women's microvascular disease [1].

Besides, from a global perspective, cardiovascular disease remains a leading cause of morbidity and mortality in young people. We should pay special attention to young female patients, whose mortality rate is still high and the risk factors are also getting worse [1]. More than 30,000 U.S. young women aged <55 years are hospitalized with AMI annually [3], among which over 15, 000 die from cardiovascular disease [4]. This specific group has higher comorbidity, longer hospital stays, and twice higher in-hospital mortality than their men counterparts [5].

Medication adherence refers to the consistency between patients' behavior and the instructions and prescriptions from health professionals [6]. Such behavior we discuss in this article is taking medication on time as directed, aimed at young women with AMI. Numerous reasons may affect

medication adherence. In terms of patient-related factors, young women with AMI have a deficiency in education level and they were sensitive to psychological pressure. With regard to socioeconomic factors, it has been reported that young women patients are likely to suffer from financial strain, which is often due to low income and high medication costs [7]. Also, social support deficit is a predictor of poor cardiac outcomes and lower quality of life (QOL) [8]. According to research, in the aspect of medical system factors, the education they receive from their health care services is predictive of prescriptions [9]. The treatment factors focus on the side effects of drug [10] and the treatment complexity [11]. Concerning technology factors, studies have found some electronic technology [12] and remote digital platforms [13] that may overcome the barrier to monitor patient compliance.

It is a fact that young women do not follow their medication well after acute myocardial infarction [14]. Smolina et al. pointed out that although the cause is unknown, the drug compliance of women with post-acute myocardial infarction aged 20-54 is indeed lower than that of men[15]. Rolnick et al. concluded that men, the elderly, and people living in areas with better education and income perform better in drug compliance with one disease [16].

Therefore, it is urgent to focus on the problem of consciously taking medicine for young women suffering from acute myocardial infarction. Although there is a lot of literature and studies discussing all influencing factors and exploring single and combined interventions, there are few summaries about this group at present. Directed at young women with AMI, in this review, we assess the relationship between drug compliance and patient-related factors, socioeconomic factors, medical system factors, treatment factors, and technology factors. The purpose of this paper is to put forward management opinions for young women and provide the guidelines for secondary prevention and medication for the clinic.

2. Patient Factors

Patient factors affecting drug compliance include age, gender, race, differences between countries and education level, psychological stress, and other factors. We will analyze the educational level and psychological stressors of young female myocardial infarction patients.

2.1 Education Level

With the development and change of China, the status of women in society has gradually improved. Both education and wages are on the rise. However, despite this positive trend, nearly 450 million of the approximately 600 million women over the age of six will be uneducated by 2020[17]. Studies have shown that there is a significant correlation between the patient's educational level and compliance. The higher the level of education, the more interested and motivated the patient is to understand the comprehensive knowledge of the disease and the main points of treatment and care, and also, appropriate level of education guarantee the ability to understand [18]. In the experiments of Cai et al [19], it was concluded that the incidence of postoperative disease in the low-level education group was obviously higher than that in the high-level group when none received relevant health education. However, when the two groups received the same health education, there was no significant difference in the incidence rate of postoperative disease between the two groups. It can be seen that the corresponding health education for patients can make up for the gap in the education of young women in China, thereby improving the drug compliance of young women.

2.2 Psychological Pressure

In China, the pressure that young women are facing comes from all aspects of life, not only do they have to work and be part of the family's economic sources, they also have to look after their parents and raise their children. They are at risk of imbalance, loneliness, and other psychological symtoms [20]. It has been reported that [20] patients suffering from the chronic disease will reduce their sense of self-control, lose their sense of self-identity, and are prone to restlessness, irritability, and other emotions. Such pressure will cause patients to create a blind escape situation, in which they are less

likely to accept the fact of the disease, thus resisting treatment. This greatly reduces drug compliance in young women. We should strengthen the psychological guidance of patients, and actively carry out corresponding psychological guidance to patients. Articles clearly point out that [21] mental health education can significantly improve the long-term compliance of myocardial infarction patients, reduce the incidence of long-term complications, improve the prognosis of patients.

3. Socioeconomic Factors

Socioeconomic status (SES), as a composite indicator of an individual's social position, primarily includes income, social support, and the overall wealth [22]. The socioeconomic factor in this review involves financial strain and social support.

3.1 Financial Strain

In this review, financial strain typically focuses on low income and high medication costs that reduce medication adherence of young women with AMI. Beckham et al. suggested that financial stressors may be a specific predictor for younger women with AMI. Compared with young men, women of the same age are presented with lower wages. As a result, they have a lower likelihood to receive health care. They are prone to postpone or even forgo their medications and therapies based on guidelines due to unaffordability[23]. Riegel et al. conducted an experiment in which a reward mechanism was applied as the intervention measure and according to the results, this has proved to be an effective incentive for patients to take medicine[24]. The study also indicated that higher socioeconomic status was independently linked to an increased distribution of meeting more cardiovascular health metrics in young women patients, such as nonsmoking, body mass index (BMI)<25kg/m², having nutritious diets following guidelines, etc[25].

Financial strain resulting from low wages and high medication costs predicted medication nonadherence. Measures such as being more accessible to affordable medications in order to offer financial protection for young women patients should be taken[25].

3.2 Social Support

With the emergence of the bio-psycho-social medical model, social support has been significantly affecting the occurrence and development of acute coronary syndrome (ACS), which may eventually lead to AMI. With sufficient social support, patients with AMI can improve their mindsets, speed up their cardiac recovery as well.

Kim et al. concluded that a dearth of social support resulted in low quality of life (QOL), and the cardiac outcomes suffer. In this case, we need more efforts and scrutiny to improve the quality of care in young women. It is worth noting that both social support and quality of life play indispensable roles in improving the heart outcomes and prognosis of young women with AMI [26].

4. Medical System Factors

The medical system consists of numerous factors, including patient education, healthcare system, and distribution of medical resources. Due to the insufficient utilization of medical resources [27], the medical system has great potential in improving drug compliance in AMI [11, 28]. For now, we discuss drug compliance from two aspects: patient education and medical resources for AMI in women.

4.1 Patient Education

Due to drug-related problems (DRP) and insufficient drug compliance [29], Jabri et al. and El Hajj et al. found that clinical pharmacists have played a key role in improving the drug compliance of patients. For example, pharmacists provide reasonable medication plans for different patients and adjust the medication plan at any time according to the daily situation of patients. In addition, during the intervention, pharmacists have the highest frequency of adding necessary drugs, followed by dose optimization and removing drug duplication. The results showed that patients' compliance with most

drugs was significantly improved, especially β blockers, angiotensin converting enzyme inhibitors (ACEI), and statins [9, 30]. It can be seen that positive communication and cooperation between doctors and pharmacists will play a great role in improving drug compliance [31]. In the treatment of AMI, we not only focus on the education of doctors to patients, but also call for the cooperation of the whole medical system. The personnel of the health system should understand compliance psychology, making comfortable responses to patients' drug decisions, and play a key role in the follow-up of secondary health care and disease rehabilitation [32].

In the medical system, few studies focused on drug compliance for young female AMI patients. However, there are also a lot studies about the current situations of young women in drug compliance. For instance, Smolina et al. found that young women are less likely to receive treatment one year after discharge than men, but there is no difference in drug compliance [15]. On the other hand, the adverse consequences of AMI in young women are higher than those in men, and the in-hospital mortality of women is 2-3 times higher than that of men [33]. In our view, improving the guidance provided by medical staff to young female patients with AMI in the treatment process will play a vital role in the future based on the current situation.

4.2 Utilization of Medical Resources

At present, the rational utilization of medical resources plays an important role in the treatment of patients with AMI. We found that the consultation rate of patients with acute coronary syndrome 6 months after discharge is greatly higher than before, which has an important impact on strengthening the prevention of primary health care [34]. Besides, community pharmacists and primary health care doctors have cooperated to make full use of local medical resources to help provide preventive health care and chronic disease management, which has played a positive role in the prognosis and treatment of patients with AMI [35]. In addition, Xavier et al. found that the intervention based on community health workers can improve the secondary prevention of coronary artery disease. This not only improves the compliance with evidence-based drugs and healthy lifestyles, but also makes more use of medical resources [36].

5. Treatment Factors

The treatment factor mainly includes the side effects of the drug and the treatment complexity [10].

5.1 Side Effect

An interview with outpatients showed that the patient refuses to take the medicine because of concerns about the side effects of the medicine or has already experienced adverse reactions [11].

There are currently several discussions or measures for the reduction in compliance caused by side effects. The first is to identify drugs suitable for young women to minimize side effects and improve compliance. Studies by Tamargo et al. have shown that women have higher drug side effects for cardiovascular drugs, which may be due to the high frequency of drug use and differences in prescription and physiology from men [37]. Zhao et al. concluded that compared with men, women use diuretics more than aspirin, statins, or ACEI [38]. Therefore, we need to monitor the safety of cardiovascular drugs based on gender and age differences, so as to formulate drug prescriptions for young women [37]. On the other hand, strengthening the drug knowledge education of young women patients as well as communication between doctors and patients also requires attention [39]. Due to a lack of drug knowledge, patients will mistakenly attribute adverse events to taking drugs, such as statins [40]. According to the American Heart Association, patients often voluntarily stop taking medications due to adverse muscle reactions caused by statins when in fact, there is no direct connection [41, 42]. Clinical trials have been designed to observe whether the compliance of patients who refuse to use statins is improved after ensuring the safety of the drugs and after adequate education [40].

5.2 Treatment Complexity

Prescriptions on AMI provided by doctors tend to be complicated, thus the time, amount, and frequency of those drugs may confuse patients, who in turn give up treatment [11, 27].

In order to solve this problem, we are exploring simplified prescriptions. The polypill combines a variety of drugs for the treatment of AMI in a fixed dose, with statins, aspirin, and beta blockers being the most common, reducing the burden on patients [43]. A number of studies have shown that it has a significant impact on reducing cardiovascular events and improving adherence [44]. From the study on polypill strategy by Roshandel et al., the experimental group using polypill has higher drug compliance, and the results are consistent between men and women, young and old [45]. However, the challenges of the polypills still exist. More clinical trials are still going on to test the clinical effect. At the same time, multi-purpose polypills with the fixed dose are not targeted at individualized solutions while the cost of single-purpose polypills are unattainable, which affects compliance [46]. Jowett et al. explored the economic cost-effectiveness of the polypill strategy according to age and gender groupings, and concluded that the most cost-effective group was women aged 40–49 [47]. Based on the good effect of polypills among young people and women, and the surprisingly high cost-effectiveness of polypills among middle-aged women, we have reasons to apply polypills to this group more broadly.

6. Technology Factors

Due to the scarcity of medical resources in certain regions, some patients cannot obtain drugs in time or have hospitals and pharmacies at their range, resulting in low adherence [11]. A study conducted by Pietrzykowski et al. showed that due to different places of accommodation, urban residents have higher drug compliance after AMI than rural residents [48].

Some electronic technology may overcome regional and traffic barriers to monitor patient compliance and secondary prevention. As a daily necessity, mobile phones play an important role in improving the compliance of patients with AMI. A systematic review by Unal et al. concluded that mobile phones have an effect on the secondary prevention of cardiovascular disease, and most of the included experimental patients have improved drug compliance [49]. A small randomized controlled experiment conducted by Akhu-Zaheya et al. also showed that the experimental group that continued to receive text messages had significant differences in medication adherence with the control group [50]. In addition to the traditional form of texting, apps and videos are equally effective. Wang et al. proposed that mobile phone applications can chart and record medication [12]. Krackhardt et al. used a new mobile app, Me & My Heart, trying to improve adherence to antiplatelet therapy in patients with acute coronary artery disease [51]. Bruggmann et al. designed a video called "Mon Coeur, Mon BASIC" that can be viewed on a smartphone and the results appeared to improve medication adherence in patients with myocardial infarction [52]. Although there are few studies on young women in this field, mobile phones and apps may be feasible and malleable to improve AMI in young women based on the influence of mobile phone intervention on the drug compliance of teenagers [53, 54]. A study by Ngaruiya et al. concluded that women are more likely to receive health text messages, so using text messages can be a fair health intervention for such groups [55].

The development of modern technology has made telemedicine and electronic platforms possible. Spaulding et al. described a platform called Corrie that try to reduce readmission rates for patients with myocardial infarction by managing drug and its side effects, recording health data, and sending educational articles [13]. The experience of a middle-aged woman with inferior ST-elevation MI that has used Carrie confirmed that it enhanced patient self-management [56]. The remote network platform built by Jameie for patients with AMI provides multiple services including self-monitoring and medication reminders for patients who cannot go to face-to-face consultation, making remote medical care more convenient [57]. The review by Gandapur et al. included 10 clinical studies that showed that mHealth improved the compliance of cardiovascular patients to different degrees [58].

Carreiro's exploration of the use of mHealth by teenagers and adults to overcome drug barriers shows that young people have a higher degree of acceptance and use of electronic technology. However, in the future, there is still a need to develop a more personalized mHealth use plan based on age and gender [59].

7. Conclusion

It can be seen that most of the factors are important for improving the drug compliance of young women with acute myocardial infarction. With the improvement of economic, political, cultural, and educational level, social institutions from all walks of life have actively helped to get rid of the economic burden. Until now, more and more young women are achieving economic independence. In addition, in the medical system, doctors, pharmacists, nurses, and other personages are not only responsible for their own fields, but also cooperate to fill in the gaps, so that medical system personnel can improve compliance by strengthening patient education and making rational use of medical resources. At the same time, it is important to correctly understand the side effects of drugs and make progress in reducing drug complexity. What is more exciting is that with the rapid development of science and technology, new approaches may be applied in the secondary prevention of AMI and drug compliance [60]. In terms of improving the drug compliance of young women with AMI, various factors are closely related and jointly affect drug compliance.

Future researches with young female groups may focus on their physiology, socioeconomic status, and actual conditions comprehensively, which may provide efficient measures to improve drug compliance. At the same time, actions should be taken from all quarters which are closely connected, including patients, families, communities, hospitals, companies, and the government.

References

[1] L. S. Mehta *et al.*, "Acute Myocardial Infarction in Women: A Scientific Statement From the American Heart Association," (in eng), *Circulation*, vol. 133, no. 9, pp. 916-47, Mar 1 2016, doi: 10.1161/cir.00000000000351.

[2] H. Akbar, C. Foth, R. A. Kahloon, and S. Mountfort, "Acute ST Elevation Myocardial Infarction," in *StatPearls*. Treasure Island (FL): StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC., 2021.

[3] B. Safdar *et al.*, "Presentation, Clinical Profile, and Prognosis of Young Patients With Myocardial Infarction With Nonobstructive Coronary Arteries (MINOCA): Results From the VIRGO Study," (in eng), *J Am Heart Assoc*, vol. 7, no. 13, Jun 28 2018, doi: 10.1161/jaha.118.009174.

[4] J. H. Lichtman *et al.*, "Symptom recognition and healthcare experiences of young women with acute myocardial infarction," (in eng), *Circ Cardiovasc Qual Outcomes*, vol. 8, no. 2 Suppl 1, pp. S31-8, Mar 2015, doi: 10.1161/circoutcomes.114.001612.

[5] R. Gulati *et al.*, "Acute Myocardial Infarction in Young Individuals," (in eng), *Mayo Clin Proc*, vol. 95, no. 1, pp. 136-156, Jan 2020, doi: 10.1016/j.mayocp.2019.05.001.

[6] M. T. Brown and J. K. Bussell, "Medication adherence: WHO cares?," (in eng), *Mayo Clin Proc*, vol. 86, no. 4, pp. 304-14, Apr 2011, doi: 10.4065/mcp.2010.0575.

[7] A. L. Beckman *et al.*, "Sex Differences in Financial Barriers and the Relationship to Recovery After Acute Myocardial Infarction," (in eng), *J Am Heart Assoc*, vol. 5, no. 10, Oct 14 2016, doi: 10.1161/jaha.116.003923.

[8] J. W. Kim *et al.*, "Social support deficit and depression treatment outcomes in patients with acute coronary syndrome: Findings from the EsDEPACS study," (in eng), *Int J Psychiatry Med*, vol. 54, no. 1, pp. 39-52, Jan 2019, doi: 10.1177/0091217418791439.

[9] A. M. Jabri, H. C. Assad, and A. A. Al-Jumaili, "Pharmacist role to enhance the prescribing of hospital discharge medications for patients after heart attack," (in eng), *Saudi Pharm J*, vol. 28, no. 4, pp. 473-479, Apr 2020, doi: 10.1016/j.jsps.2020.02.009.

[10] H. Xu, H. Hu, and M. Li, "Review of foreign studies on drug compliance barriers "*Chinese Pharmacy* vol. 29, no. 19, pp. 2723 - 2727, 2018.

[11] F. L. Mondesir *et al.*, "Patient Perspectives on Factors Influencing Medication Adherence Among People with Coronary Heart Disease (CHD) and CHD Risk Factors," (in eng), *Patient preference and adherence*, vol. 13, pp. 2017-2027, 2019, doi: 10.2147/ppa.S222176.

[12] J. Wang, S. Wongvibulsin, K. Henry, and S. Fujita, "Quantifying and Visualizing Medication Adherence in Patients Following Acute Myocardial Infarction," (in eng), *AMIA Annu Symp Proc*, vol. 2017, pp. 2299-2303, 2017.

[13] E. M. Spaulding *et al.*, "Corrie Health Digital Platform for Self-Management in Secondary Prevention After Acute Myocardial Infarction," (in eng), *Circ Cardiovasc Qual Outcomes*, vol. 12, no. 5, p. e005509, May 2019, doi: 10.1161/circoutcomes.119.005509.

[14] M. Davis, J. Diamond, D. Montgomery, S. Krishnan, K. Eagle, and E. Jackson, "Acute coronary syndrome in young women under 55 years of age: clinical characteristics, treatment, and outcomes," (in eng), *Clin Res Cardiol*, vol. 104, no. 8, pp. 648-55, Aug 2015, doi: 10.1007/s00392-015-0827-2.

[15] K. Smolina, L. Ball, K. H. Humphries, N. Khan, and S. G. Morgan, "Sex Disparities in Post-Acute Myocardial Infarction Pharmacologic Treatment Initiation and Adherence: Problem for Young Women," (in eng), *Circ Cardiovasc Qual Outcomes*, vol. 8, no. 6, pp. 586-92, Nov 2015, doi: 10.1161/circoutcomes.115.001987.

[16] S. J. Rolnick, P. A. Pawloski, B. D. Hedblom, S. E. Asche, and R. J. Bruzek, "Patient characteristics associated with medication adherence," (in eng), *Clin Med Res*, vol. 11, no. 2, pp. 54-65, Jun 2013, doi: 10.3121/cmr.2013.1113.

[17] Y. Wu *et al.*, "Effect of a Quality of Care Improvement Initiative in Patients With Acute Coronary Syndrome in Resource-Constrained Hospitals in China: A Randomized Clinical Trial," (in eng), *JAMA Cardiol*, vol. 4, no. 5, pp. 418-427, May 1 2019, doi: 10.1001/jamacardio.2019.0897.

[18] L. Zhu, H. Lu, and Y. Xu, "Analysis of anxiety and depression in acute and convalescent period of myocardial infarction patients.," *Shanghai Nursing*, vol. 13, no.5, 2013, doi: 1009-8399(2013)05-0009 - 04.

[19] Q. Cai and L. Gu, "Influence of education level on health education of patients undergoing cardiac surgery.," *International Medical and Health Guide*, vol. 19, No.1, 2013, doi: 1007-1245.2013.01.046.

[20] F. Lin and H. Hu, "The relationship between self-identity and mental health in middle-aged women with chronic diseases.," *Mother and Child World*, vol. 13, No.01, 2018, doi: 1671-2242 (2018) 13 - 0289 - 01.

[21] J. X. Z. Y. Zhang, "Effect of health education on medication compliance of patients with myocardial infarction.," *Psychological Doctor*, vol. 16, No.3, 2016, doi: 1007-8231 (2016) 16-0150-03.

[22] D. Tousoulis, E. Oikonomou, G. Vogiatzi, and P. Vardas, "Cardiovascular disease and socioeconomic status," (in eng), *Eur Heart J*, vol. 41, no. 34, pp. 3213-3214, Sep 7 2020, doi: 10.1093/eurheartj/ehaa405.

[23] B. Riegel, A. Stephens-Shields, A. Jaskowiak-Barr, M. Daus, and S. E. Kimmel, "A behavioral economics-based telehealth intervention to improve aspirin adherence following hospitalization for

acute coronary syndrome," (in eng), *Pharmacoepidemiol Drug Saf*, vol. 29, no. 5, pp. 513-517, May 2020, doi: 10.1002/pds.4988.

[24] J. Ren *et al.*, "Ideal cardiovascular health status and its association with socioeconomic factors in Chinese adults in Shandong, China," (in eng), *BMC Public Health*, vol. 16, no. 1, p. 942, Sep 7 2016, doi: 10.1186/s12889 - 016 - 3632 - 6.

[25] C. Y. Osborn, S. Kripalani, K. M. Goggins, and K. A. Wallston, "Financial strain is associated with medication nonadherence and worse self-rated health among cardiovascular patients," (in eng), *J Health Care Poor Underserved*, vol. 28, no. 1, pp. 499-513, 2017, doi: 10.1353/hpu.2017.0036.

[26] Y. Feng, J. Liang, and B. Yang, "Correlation between social support and quality of life in patients with acute myocardial infarction," *Journal of Wuhan University (Medical Science)*, vol. 33, no. 02, pp. 251 - 254, 2012.

[27] F. Devine, T. Edwards, and S. R. Feldman, "Barriers to treatment: describing them from a different perspective," (in eng), *Patient Prefer Adherence*, vol. 12, pp. 129-133, 2018, doi: 10.2147/ppa.S147420.

[28] N. R. Desai and N. K. Choudhry, "Impediments to adherence to post myocardial infarction medications," (in eng), *Curr Cardiol Rep*, vol. 15, no. 1, p. 322, Jan 2013, doi: 10.1007/s11886-012-0322 - 6.

[29] E. A. Casper, L. M. El Wakeel, M. A. Saleh, and M. H. El-Hamamsy, "Management of pharmacotherapy-related problems in acute coronary syndrome: Role of clinical pharmacist in cardiac rehabilitation unit," (in eng), *Basic Clin Pharmacol Toxicol*, vol. 125, no. 1, pp. 44-53, Jul 2019, doi: 10.1111/bcpt.13210.

[30] M. S. El Hajj, M. J. Jaam, and A. Awaisu, "Effect of pharmacist care on medication adherence and cardiovascular outcomes among patients post-acute coronary syndrome: A systematic review," (in eng), *Research in social & administrative pharmacy : RSAP*, vol. 14, no. 6, pp. 507-520, Jun 2018, doi: 10.1016/j.sapharm.2017.06.004.

[31] D. Swieczkowski *et al.*, "Medication adherence in patients after percutaneous coronary intervention due to acute myocardial infarction: From research to clinical implications," (in eng), *Cardiol J*, vol. 23, no. 5, pp. 483-490, 2016, doi: 10.5603/CJ.a2016.0048.

[32] J. Keenan, "Improving adherence to medication for secondary cardiovascular disease prevention," (in eng), *Eur J Prev Cardiol*, vol. 24, no. 3_suppl, pp. 29-35, Jun 2017, doi: 10.1177/2047487317708145.

[33] E. M. Bucholz *et al.*, "Editor's Choice-Sex differences in young patients with acute myocardial infarction: A VIRGO study analysis," (in eng), *Eur Heart J Acute Cardiovasc Care*, vol. 6, no. 7, pp. 610-622, Oct 2017, doi: 10.1177/2048872616661847.

[34] K. Hyun *et al.*, "Impact of medical consultation frequency on risk factors and medications 6 months after acute coronary syndrome," (in eng), *Public Health Res Pract*, vol. 26, no. 1, p. e2611606, Jan 28 2016, doi: 10.17061/phrp2611606.

[35] L. A. Berenbrok, N. Gabriel, K. C. Coley, and I. Hernandez, "Evaluation of Frequency of Encounters With Primary Care Physicians vs Visits to Community Pharmacies Among Medicare Beneficiaries," (in eng), *JAMA Netw Open*, vol. 3, no. 7, p. e209132, Jul 1 2020, doi: 10.1001/jamanetworkopen.2020.9132.

[36] D. Xavier *et al.*, "Community health worker-based intervention for adherence to drugs and lifestyle change after acute coronary syndrome: a multicentre, open, randomised controlled trial," (in eng), *Lancet Diabetes Endocrinol*, vol. 4, no. 3, pp. 244-253, Mar 2016, doi: 10.1016/s2213 - 8587 (15) 00480 - 5.

[37] J. Tamargo *et al.*, "Gender differences in the effects of cardiovascular drugs," (in eng), *Eur Heart J Cardiovasc Pharmacother*, vol. 3, no. 3, pp. 163-182, Jul 1 2017, doi: 10.1093/ehjcvp/pvw042.

[38] M. Zhao *et al.*, "Sex Differences in Cardiovascular Medication Prescription in Primary Care: A Systematic Review and Meta-Analysis," (in eng), *J Am Heart Assoc*, vol. 9, no. 11, p. e014742, Jun 2 2020, doi: 10.1161/jaha.119.014742.

[39] X. Fu, Y. Wan, H. Wang, L. Zhang, and X. Ma, "Comparative analysis of the effect of statin compliance on the prognosis of patients with myocardial infarction and cerebral infarction," *Chinese Journal of Evidence-Based Cardiovascular Medicine*, vol. 12, no. 07, pp. 877-881, 2020.

[40] K. Tudor, J. Brooks, J. Howick, R. Fox, and P. Aveyard, "Tackling statin intolerance with n-of-1 trials (TaSINI) in primary care: protocol for a feasibility randomised trial to increase statin adherence," (in eng), *BMJ open*, vol. 10, no. 2, p. e033070, Feb 12 2020, doi: 10.1136/bmjopen-2019-033070.

[41] C. B. Newman *et al.*, "Statin Safety and Associated Adverse Events: A Scientific Statement From the American Heart Association," (in eng), *Arteriosclerosis, thrombosis, and vascular biology*, vol. 39, no. 2, pp. e38-e81, Feb 2019, doi: 10.1161/atv.000000000000073.

[42] T. Cai *et al.*, "Associations between statins and adverse events in primary prevention of cardiovascular disease: systematic review with pairwise, network, and dose-response meta-analyses," (in eng), *BMJ (Clinical research ed.)*, vol. 374, p. n1537, Jul 14 2021, doi: 10.1136/bmj.n1537.

[43] P. Bramlage, H. Sims, J. Minguet, and C. Ferrero, "The polypill: An effective approach to increasing adherence and reducing cardiovascular event risk," (in eng), *European journal of preventive cardiology*, vol. 24, no. 3, pp. 297-310, Feb 2017, doi: 10.1177/2047487316674817.

[44] P. Bramlage *et al.*, "[Management of different cardiovascular risk factors with a combination tablet (polypill)]," (in ger), *Herz*, vol. 43, no. 3, pp. 246-257, May 2018, doi: 10.1007/s00059-017-4554-5. Management verschiedener kardiovaskulärer Risikofaktoren mit einem Kombinationspräparat ("Polypill").

[45] G. Roshandel *et al.*, "Effectiveness of polypill for primary and secondary prevention of cardiovascular diseases (PolyIran): a pragmatic, cluster-randomised trial," (in eng), *Lancet*, vol. 394, no. 10199, pp. 672-683, Aug 24 2019, doi: 10.1016/s0140-6736(19)31791-x.

[46] A. Sukonthasarn *et al.*, "The feasibility of polypill for cardiovascular disease prevention in Asian Population," (in eng), *Journal of clinical hypertension (Greenwich, Conn.)*, vol. 23, no. 3, pp. 545-555, Mar 2021, doi: 10.1111/jch.14075.

[47] S. Jowett *et al.*, "Cost-effectiveness analysis of use of a polypill versus usual care or best practice for primary prevention in people at high risk of cardiovascular disease," (in eng), *PLoS One*, vol. 12, no. 9, p. e0182625, 2017, doi: 10.1371/journal.pone.0182625.

[48] Ł. Pietrzykowski *et al.*, "Medication adherence and its determinants in patients after myocardial infarction," (in eng), *Scientific reports*, vol. 10, no. 1, p. 12028, Jul 21 2020, doi: 10.1038/s41598-020 - 68915 - 1.

[49] E. Unal, K. Giakoumidakis, E. Khan, and E. Patelarou, "Mobile phone text messaging for improving secondary prevention in cardiovascular diseases: A systematic review," (in eng), *Heart Lung*, vol. 47, no. 4, pp. 351-359, Jul-Aug 2018, doi: 10.1016/j.hrtlng.2018.05.009.

[50] L. M. Akhu-Zaheya and W. Y. Shiyab, "The effect of short message system (SMS) reminder on adherence to a healthy diet, medication, and cessation of smoking among adult patients with cardiovascular diseases," (in eng), *Int J Med Inform*, vol. 98, pp. 65-75, Feb 2017, doi: 10.1016/j.ijmedinf.2016.12.003.

[51] F. Krackhardt *et al.*, "Design and rationale for the "Me & My Heart" (eMocial) study: A randomized evaluation of a new smartphone-based support tool to increase therapy adherence of patients with acute coronary syndrome," (in eng), *Clinical cardiology*, vol. 42, no. 11, pp. 1054-1062, Nov 2019, doi: 10.1002/clc.23254.

[52] C. Bruggmann, J. Adjedj, S. Sardy, O. Muller, P. Voirol, and F. Sadeghipour, "Effects of the Interactive Web-Based Video "Mon Coeur, Mon BASIC" on Drug Adherence of Patients With Myocardial Infarction: Randomized Controlled Trial," (in eng), *J Med Internet Res*, vol. 23, no. 8, p. e21938, Aug 30 2021, doi: 10.2196/21938.

[53] S. M. Badawy S, Kaviany S., "Text messaging and smartphone app interventions to improve adherence in adolescents and young adults: a systematic review and meta-analysis.," 2017-03-28.

[54] S. M. Badawy, L. Barrera, M. G. Sinno, S. Kaviany, L. C. O'Dwyer, and L. M. Kuhns, "Text Messaging and Mobile Phone Apps as Interventions to Improve Adherence in Adolescents With Chronic Health Conditions: A Systematic Review," (in eng), *JMIR Mhealth Uhealth*, vol. 5, no. 5, p. e66, May 15 2017, doi: 10.2196/mhealth.7798.

[55] C. Ngaruiya, S. Oti, S. van de Vijver, C. Kyobutungi, and C. Free, "Target women: Equity in access to mHealth technology in a non-communicable disease care intervention in Kenya," (in eng), PLoS *One*, vol. 14, no. 9, p. e0220834, 2019, doi: 10.1371/journal.pone.0220834.

[56] G. Hung, W. E. Yang, F. A. Marvel, and S. S. Martin, "Mobile health application platform 'Corrie' personalises and empowers the heart attack recovery patient experience in the hospital and at home for an underserved heart attack survivor," (in eng), *BMJ Case Rep*, vol. 13, no. 2, Feb 17 2020, doi: 10.1136/bcr - 2019 - 231801.

[57] S. Jameie, H. Haybar, A. Aslani, and M. Saadat, "Development and Usability Evaluation of Web-Based Telerehabilitation Platform for Patients After Myocardial Infarction," (in eng), *Studies in health technology and informatics*, vol. 261, pp. 68 - 74, 2019.

[58] Y. Gandapur *et al.*, "The role of mHealth for improving medication adherence in patients with cardiovascular disease: a systematic review," (in eng), *European heart journal. Quality of care & clinical outcomes*, vol. 2, no. 4, pp. 237-244, Oct 1 2016, doi: 10.1093/ehjqcco/qcw018.

[59] S. Carreiro, P. R. Chai, J. Carey, J. Lai, D. Smelson, and E. W. Boyer, "mHealth for the Detection and Intervention in Adolescent and Young Adult Substance Use Disorder," (in eng), *Curr Addict Rep*, vol. 5, no. 2, pp. 110-119, Jun 2018, doi: 10.1007/s40429-018-0192-0.

[60] P. M. Ho *et al.*, "Multifaceted intervention to improve medication adherence and secondary prevention measures after acute coronary syndrome hospital discharge: a randomized clinical trial," (in eng), *JAMA Intern Med*, vol. 174, no. 2, pp. 186-93, Feb 1 2014, doi: 10.1001/jamainternmed.2013.12944.