SYSTEMATIC REVIEW

Medication adherence and racial differences in diabetes in the USA: an update

Diabetes Management



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Practice points

- Rates of nonadherence by race/ethnicity persist over time. Racial and ethnic differences in adherence persist across various settings of care. For patients using concurrent therapies to address cardiovascular risk, monitoring of primary nonadherence may be especially important.
- Mediators/underlying determinants of disparities in adherence. Race and ethnicity are not accurate predictors of future nonadherence. However, health literacy, medication concerns and medication costs may be important mediators for black and Latino patients.
- System and policy-level interventions to address disparities. There is a need for more interventions designed to
 reduce disparities in medication adherence and diabetes control. Health systems that have electronic health records
 are well poised to conduct experimental and quasi-experimental studies to evaluate the effectiveness of different
 strategies aimed at addressing modifiable determinants of these disparities.

SUMMARY Rates of diabetes medication adherence are suboptimal among disparities populations. This review explores the latest evidence regarding racial and ethnic differences in medication adherence. We conducted a comprehensive search of the PubMed database for articles published between January 2007 and June 2014. We included observational and interventional studies exploring racial and ethnic differences in medication adherence in diabetes. Of the studies, 38 met inclusion criteria and provided consistent evidence of persistent disparities in adherence. Potential mediators included health literacy, medication concerns and medication costs. There is a paucity of evidence regarding successful strategies to reduce disparities in adherence and outcomes. More well-designed experiments and quasi-experiments designed to address potential mediators of disparities in adherence are needed.

Diabetes mellitus affects 29.1 million Americans and costs an estimated US\$245 billion per year in healthcare costs and lost productivity [1]. Management of blood sugar levels and related risk factors is critical to the secondary prevention of potentially disabling and life-threatening complications [2]. Oral hypoglycemic medications and insulin have demonstrated efficacy in achieving clinically meaningful reductions in glycemic control and corresponding microvascular events. In addition, pharmacologic co-management of cardiovascular risk factors including hypertension and hyperlipidemia reduces the risk of potentially life-threatening cardiovascular events among

KEYWORDS

- diabetes disparities
- medication adherence
- race and ethnicity

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patients with diabetes. More recently, studies have begun exploring whether pharmacologic co-management of common comorbidities such as depression can improve both diabetes specific outcomes and overall patient quality of life [2].

Despite the promise of prescription medications to improve diabetes control and outcomes, nonadherence remains a persistent problem [3]. Addressing suboptimal adherence is a critical focus of clinical interventions because of the potential impact on glycemic control and ignoring nonadherence may lead to the unnecessary addition of a new drug [4]. Identifying modifiable factors associated with nonadherence is critical to creating effective interventions to address it.

Factors associated with nonadherence are varied and likely include attributes of the medication regimen (e.g., out of pocket costs, side effects, complexity, frequency of administration), characteristics of patients (e.g., self-efficacy, beliefs about the safety and efficacy of medications, comorbid depression) and characteristics of the healthcare system (e.g., physician beliefs about patient commitment to adherence, lack of follow-up) [5]. Of particular concern are persistent findings of non-modifiable factors associated with adherence, particularly patient race and ethnicity [6]. In 2007, Heisler and colleagues published a study suggesting that lower medication adherence among blacks may contribute to disparities in control [7]. However, limitations in the available literature such as small sample size and a reliance on cross-sectional descriptive analyses and self-reported adherence inhibited the further exploration of explanatory factors and changes in adherence over time [5,7-10].

In that same year, a review of diabetes interventions to reduce disparities reported that nurse-led case management interventions hold the most promise in terms of improving medication adherence [11]. However, the authors also identified gaps in the intervention literature including the absence of studies focused on Native American, Asian subgroups, and the very old and the very young. In addition, the majority of interventions focused on a single subgroup of patients. As a consequence, only two of the more than 40 interventions identified examined the impact of the intervention on racial and ethnic disparities in self-care practices or outcomes [11].

The purpose of this update is to assess how far we have come since 2007 in our understanding of persistent racial and ethnic differences in medication adherence and how to address this critical gap in diabetes management. We pay special attention to the state of the science with respect to the use of research methods that have the greatest potential to yield strong evidence to guide clinical practice and health system response to these disparities.

Methods

We conducted a comprehensive search of the PubMed database using the search terms: diabetes, medication, race, adherence, compliance and combinations thereof. In addition, we used published reviews and the reference section of published articles to identify additional studies. We included studies of patients with both Type 1 and 2 diabetes, but also included studies in which a subset of the population had diabetes as long as those studies included adherence to diabetes-related medications. Only quantitative studies conducted in the USA and published between 1 January 2007 and 30 June 2014 were included. We further excluded those studies that focused on a single or predominant race or ethnicity as these did not permit the exploration of differences across subgroups.

Articles meeting our criteria based on abstract review were extracted for confirmation of eligibility and categorization of study design characteristics. We used well-established guidelines for assessing the quality of studies to code the articles [12–14]. Two of the authors (AS Adams, S Banerjee) worked independently to code each of the identified studies.

Results

Characteristics of included studies

Our search identified 113 articles, 38 of which met our inclusion criteria (**Table 1**), including 21 cross-sectional studies, [7,15–34] 14 retrospective longitudinal cohort studies, [35–47] 1 prospective longitudinal cohort study, [48] 1 natural experiment [49] and 1 randomized controlled trial [37]. Of the studies, 19 used self-reported measures of medication adherence; previously validated instruments such as the Morisky scale and cost-related nonadherence were used most frequently. The remaining studies relied on pharmacy claims, electronic health records or a combination of both to assess adherence.

Table 1. Racial/ethnic differences in primary nonadherence among studies meeting inclusion criteria.										
Study (year)	n	Population	Race/ethnic subgroups	Oral diabetes medications	Antihypersensitives	Lipid-lowering	Ref.			
				Significant differences in risk/odds of primary nonadherence		agents				
Lora <i>et al.</i> (2013)	27,539	Illinois public aid program (Medicaid)	Black, white, Spanish- speaking Latinos, English-speaking Latinos	-	Blacks, English- speaking Latinos and Spanish-speaking Latinos had lower rates of nonadherence relative to whites	-	[28]			
Raebel <i>et al.</i> (2012)	10,919	Integrated healthcare delivery system	No difference Whites, Latinos, other, unknown	No difference	Latinos and patients of other or unknown race/ethnicity had higher rates of nonadherence relative to whites	Latinos had higher rates of nonadherence relative to whites	[36]			
Trinacty <i>et al.</i> (2009)	1906	Multi-specialty care group	Whites, blacks	No difference	-	-	[45]			

• Rates of nonadherence by race/ethnicity and persistence over time

Figure 1 describes the distribution of studies reporting statistically significant differences in adherence by race and ethnicity. The majority of studies comparing medication adherence among white patients with African-American [7,15-17,19,23,25-26,28-32,34-35,37-42,44-45,48] and Latino patients [7,24,28,30-31,33-35,38-42] reported significantly lower rates of adherence compared with whites. One study reported that non English-speaking Latinos are at greater risk for nonadherence than those who speak English [28]. Among the nine studies including comparisons of Asians with other racial and ethnic subgroups, only four reported lower rates of adherence among Asians and two of these were driven by lower rates of adherence among Filipinos. Three studies reported better adherence among Asian subgroups (Japanese, Vietnamese). Native Americans, Alaskan Natives and Native Hawaiians [34,39,43,47] continue to be underrepresented in studies of adherence, but showed consistently higher rates of nonadherence.

In recent years, several studies have leveraged the power of longitudinal claims and electronic medical record data to examine racial and ethnic differences in adherence over time. The availability of these data allows researchers to isolate individual stages of adherence, including primary nonadherence (i.e., picking up a prescribed medication) and long-term persistence [50–52]. **Table 1** shows the results of studying examining disparities in primary nonadherence. Two independent studies reported that race and ethnicity

were not associated with primary nonadherence to diabetes-specific medications (insulin, oral hypoglycemic medications) [36,45]. However, studies examining primary nonadherence related to antihypertensive and lipid-lowering therapy among patients with diabetes reported conflicting evidence. For example, Lora and colleagues found that blacks and Latinos (English- and Spanish-speaking) in a State of Illinois Public Aid program were more likely to fill a prescription for an ace inhibitor or an angiotensin receptor blocker relative to whites regardless of gender [28]. In contrast, among patients in an integrated healthcare system, Raebel and colleagues reported that Latinos were less likely to fill a prescription (i.e., primary nonadherence) for both antihypertensives and lipid-lowering therapy compared with non-Latino whites [36].

We found strong evidence of disparities in long-term adherence across multiple types of medications and controlling for demographic and clinical confounders [37-42,44-45,47]. Trinacty and colleagues also found higher rates of discontinuation of oral diabetes medications among black and white diabetes patients in a multispecialty care group Boston who were newly prescribed medications [45].

• Medication adherence as a mediator of disparities in control

We identified few studies that examined medication adherence as a mediator of disparities in diabetes clinical outcomes (Figure 2). One of the authors of this review (AS Adams) published a study in 2008 in which we estimated that closing

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Figure 1. Distribution of identified studies by race/ethnic subgroup of interest and evidence of disparities in medication adherence.

the adherence gap would reduce the disparity in A1c control by at least 0.02 percentage points [50]. Reductions in A1c as small as 0.01 percentage points have been associated with statistically significant reductions in risk of diabetes complications [51]. Three other studies reported attenuation of the race effect on A1c after controlling for medication adherence [15,25,44], lending support to medication adherence as a potential mechanism for reducing disparities in outcomes.

We identified only one study that examined the relationship between medication adherence and mortality risk [46]. Among a national cohort of veterans, Hunt and colleagues reported that nonadherence to diabetes medications was associated with increased mortality risk for diabetes patients regardless of race or ethnicity. Among patients whose A1c levels were outside the target associated with the greatest increase in mortality risk for Latinos (hazard ratio: 4.45 [3.98–4.97]) relative to all other racial and ethnic groups. Latinos were also least likely to be taking any diabetes medications (<30%) over 5 years of observation [46].

• Mediators/underlying determinants of disparities in adherence

Understanding persistent racial and ethnic differences in medication adherence, an important predictor of A1c control, is essential for the development of appropriate interventions. **Figure 1** shows the relationship between race and ethnicity and medication adherence as mediated by factors that may or may not be modifiable through health system intervention. For example, studies of family support have found a positive association between a supportive home environment and diabetes adherence [18,27]. Yet, it is unclear how effective health system interventions can be in changing family dynamics. Therefore, research has increasingly focused on mediating factors that are potentially modifiable such as health literacy, language barriers, clinical support services and the patient-provider relationship. **Table 2** provides a brief summary of evidence regarding three modifiable determinants of disparities in adherence that are described in greater detail below.

Health literacy/knowledge

The ability of patients to understand relevant health information, including prescription instructions, may pose a barrier to adherence. Health literacy deficits are strongly linked with education and, therefore, may be more prevalent in some populations subgroups [5,6]. Using Path analysis, Osborn and colleagues [32] demonstrated the potential strength of this potential mediator of disparities in medication adherence by reporting the complete elimination of racial differences in medication adherence between 383 blacks and whites with diabetes after controlling for health literacy.

Medication beliefs & concerns

Patient beliefs and perceptions of the safety of medications may also influence medication taking behavior. We identified three studies that explored racial and ethnic differences in attitudes toward specific medication characteristics [15–16,21]. All three reported racial and ethnic differences in beliefs about medications, where black and Latino patients were more likely to express concerns about the complexity of medication regimens, side effects and addiction [15-16,21]. For example, in a survey of 806 black and white patients receiving care from the safety net system in Flint, Michigan, Piette and colleagues reported that blacks were more likely to endorse beliefs about medications that are consistent with suboptimal medication use such as 'People who take prescription medications should stop their treatment for a while every now and again', 'Most prescription medications are addictive' and 'Prescription medications do more harm than good'. Interestingly, these difference in beliefs did not attenuate racial differences in adherence [16].

Financial burden of medications

Racial and ethnic differences in medication adherence may be partly explained by ability to pay out-of-pocket for medications. Cost-related nonadherence (CRN) is directly related to the number and attributes of medications (e.g., cost, purpose of medication) that patients are taking. Therefore, to the extent that some racial and ethnic subgroups have higher medication burden, we might expect them to have higher reported CRN. Four out of five studies examining different aspects of CRN (e.g., failing to pick up a medication due to cost, splitting pills to make medication last longer) have demonstrated racial and ethnic differences in reported CRN among blacks and Latinos [16,24,30,33]. In a study conducted at the University of California Irvine, Ngo-Metzger and Kaplan reported stark differences in the unadjusted prevalence of CRN among diabetes patients. Specifically, while an estimated 27% of white and Vietnamese patients reported CRN, more than 50% of Mexican–Americans reported nonadherence due to cost [33].

• System & policy-level interventions to address disparities

Interventions aimed at addressing these and other modifiable determinants of disparities in medication adherence have the potential to reduce both gaps in adherence, as well as disparities in diabetes control. We identified only one completed randomized controlled trial that aimed to evaluate the impact of the intervention on disparities in adherence by race and ethnicity [53]. The goal of the IDEATel study was to evaluate the impact of telemedicine case management versus usual care on diabetes self-care practices and A1c control. The study included 1665 white, black and Latino diabetes patients with Medicare coverage. Trief and colleagues reported that self-reported adherence improved for the treatment group relative to usual care and that all racial and ethnic



Figure 2. Mediators of the relationship between race/ethnicity, medication adherence and clinical outcomes in diabetes.

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Table 2. Mediators of racial differences in medication adherence in diabetes.									
Mediators	Study (year)	Differences by race and ethnicity	Ref.						
Health literacy	Osborn <i>et al.</i> (2011)	Health literacy completely explained adherence differences between black and white patients	[32]						
Medication concerns	Duru <i>et al</i> .(2009) Piette <i>et al</i> .(2010) Huang <i>et al</i> . (2009)	Relative to white patients, blacks were more likely than whites to report dislike of medications or side effects, beliefs that medications are addictive and do more harm than good, and a distrust of generic medications relative to brand medications; However, these beliefs may not explain differences in medication adherence.	[15] [16] [21]						
Financial burden	Piette <i>et al.</i> (2010) Kaplan <i>et al.</i> (2013) Tseng <i>et al.</i> (2008) Williams <i>et al.</i> (2013) Osborn <i>et al.</i> (2011)	Black and Latino patients may be at higher risk for cost-related underuse of medicines	[16] [24] [30] [31] [32]						

subgroups improved. However, minority patients remained at a lower adherence level compared with whites, suggesting that while equally effective in all three groups, the intervention was not sufficient to close the gap in adherence [53].

In a natural experiment, Wong and colleagues evaluated the impact of increased medication copayments on racial differences in medication adherence [49]. In the 12-month period immediately following the copay increase, both white and black patients experienced a statistically significant decrease in diabetes medication adherence. These changes were even more pronounced 1 year later. However, the white–black difference in the change in adherence following the copay increase was not statistically significant in the short- or long-term follow-up periods [49].

Discussion

• Summary of the evidence

Despite increasing awareness of disparities in recent years, disparities in medication adherence persist across a broad range of racial and ethnic subgroups with diabetes. Moreover, while the magnitude of these differences may vary across types of medication, they are nonetheless persistent over time. For example, while we found no evidence of black–white disparities in primary nonadherence to diabetes medications, more evidence is needed to determine whether primary nonadherence is a problem for antihypertensives, lipid-lowering agents and other related treatments.

We found consistent evidence of persistent disparities over time among patients established

on therapy, including evidence of greater premature discontinuation of therapy among some subgroups. In addition, the latest evidence suggests that addressing disparities in medication adherence for diabetes medications has the potential to reduce disparities in diabetes control and mortality.

Importantly, health literacy and medication costs may mediate the relationship between race/ethnicity and adherence and are therefore potential targets for interventions designed to address these disparities. Findings related to medication concerns suggest that at least some amount of nonadherence among black and Latino patients may be intentional. More evidence is needed regarding the relative contribution of these factors to disparities in adherence and the extent to which they are modifiable through health system intervention.

More experimental and quasi-experimental evidence is needed to identify which strategies for addressing these barriers are most effective at reducing known disparities in adherence. The one clinical trial we included found that while a telemedicine intervention was equally effective in whites, black and Latino diabetes patients, it had no impact on pre-existing disparities in adherence [53]. Similarly, a natural experiment found that increasing medication copayment dampened adherence equally among white and black veterans [49]. Extending this logic further, we might hypothesize that reducing copayments would be equally beneficial across subgroups. However, in a recent study of the effects of Medicare Part D, we reported that white dual enrollees with

diabetes were more likely to take advantage of an expansion in medication coverage compared with blacks, resulting in an increase in pre-existing disparities in use of clinically effective lipid-lowering agents [54]. The evaluation of natural experiences in coverage change is needed to better understand copayments as a determinant and potential tool for addressing disparities in adherence in diabetes.

We also observed important advances in the quality of evidence relative to earlier studies, including increasingly diverse study populations and an effort to move beyond identifying disparities to trying to understanding them using mediational analysis techniques and previously validated measures designed to assess specific medicationtaking practices (e.g., CRN) [55,56]. While there was still a high reliance on self-reported measures of adherence, there was increased consistency in the use of previously validated measures of adherence [57]. In addition, the advent of electronic medical records and large automated claims databases have enabled researchers to investigate beyond the prevalence of adherence disparities to identify specific stages at which the subgroups diverge. Still, Native Americans, Native Hawaiians and Alaskan Natives, as well as subgroups of Asians and Latinos continued to be understudied, highlighting the need for improvement in the accurate collection of data on these subgroups.

• Limitations

This review has its limitations. We restricted our search to articles listed in PubMed and our findings are therefore prone to publication bias [57]. Moreover, we excluded studies that only included a single race or ethnic subgroup. However, this exclusion allowed us to focus on studies that had the potential to inform disparities reduction. Lastly, our review focused on medication adherence, only one part of the complex diabetes self-management regimen.

Conclusion

Medication adherence is an important and potentially modifiable determinant of disparities in diabetes outcomes across a broad range of racial and ethnic subgroups and care settings. Access to eletronic health records and other longitudinal data sources has greatly improved our ability to understand patterns in adherence over time in increasingly diverse patient populations and to identify opportunities for clinical intervention. Research to date suggests that addressing health literature and out-of-pocket costs for prescription medications are important components of any strategy for addressing disparities in adherence. However, strong experimental and quasi-experimental evidence of the effect of these and other strategies on disparities is still lacking. Making inroads to address persistent disparities in diabetes medication management will require a bold departure from weaker study designs and the move toward more rigorous and innovative research models.

Future perspective

More than 11 years after the IOM's Unequal Treatment report, we have made significant progress in our ability to identify disparities in mediation adherence in diabetes [58]. However, knowing that race and ethnicity are persistently associated with risk of nonadherence in diabetes does not move the needle in terms of finding strategies for addressing these differences [14]. Importantly, race and ethnicity are not especially useful to providers and healthcare systems as indicators of future nonadherence [59]. To address disparities in outcomes associated with nonadherence, we need to address modifiable mediators of these relationships. Our review suggests that interventions aimed at patient-specific barriers such as health literacy, medication beliefs and medication costs have the potential to directly impact disparities in adherence and related outcomes for diverse clinical populations. Future studies of these factors will need to include increasingly diverse subgroups of patients (e.g., ethnicity, language proficiency) to confirm that the relationships shown in these earlier studies hold true across populations. In addition, studies are needed to investigate additional health system factors, such as patient-provider communication and access to self-care support, as targets for intervention. Importantly, directly testing the impact of new interventions on disparities in medication adherence and subsequent diabetes outcomes are needed to assess their ability to drive us toward more equitable healthcare outcomes.

Disclaimer

We declare that all of the authors meet minimal criteria for inclusion as co-authors, the funders had no role in the design, writing or editing of this paper, and that this manuscript is not under consideration by any other journal.

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