“The Point”
ZSFG Diabetes Newsletter - October 2018

Making diabetes care easier, better, less frustrating and more fun since 2008

TOPICS:

New SharePoint website for ZSFG diabetes resources

Making sense of diabetes medications

Welcome Diabetes team’s newest member

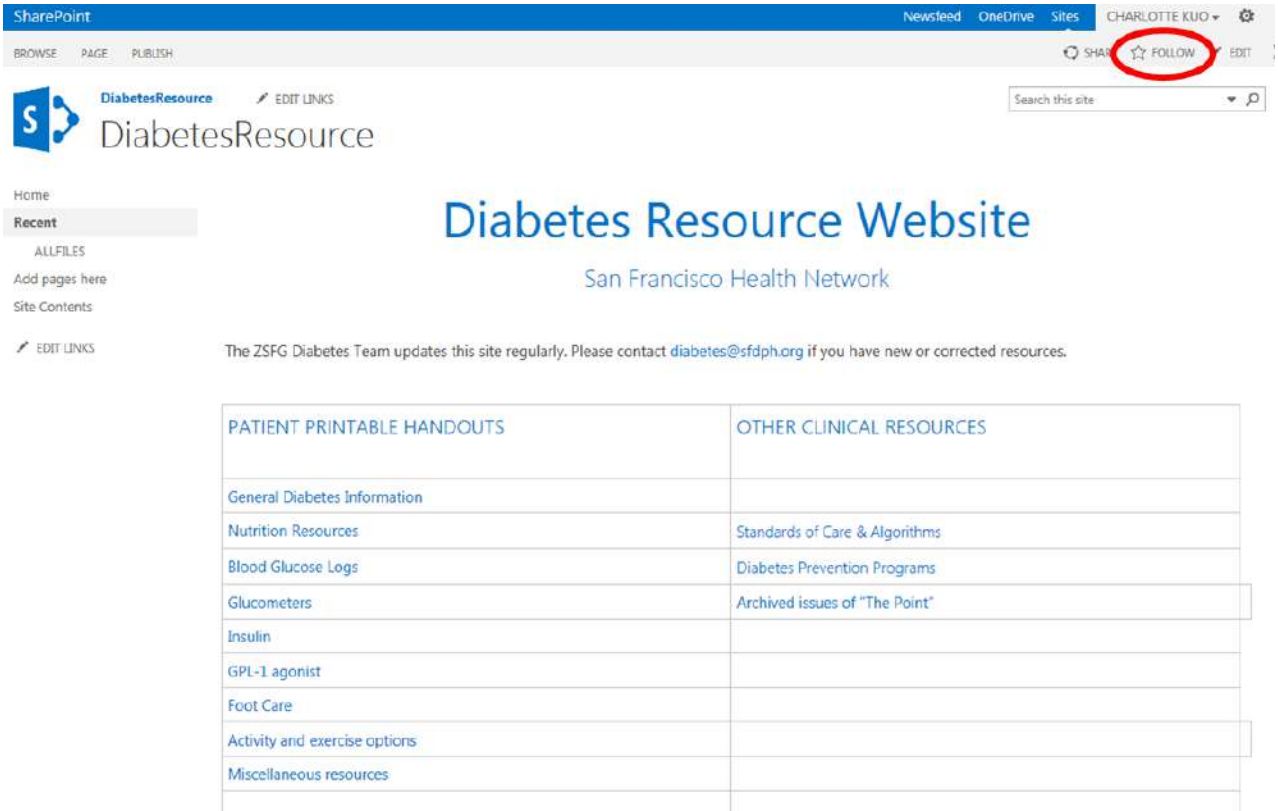
New diabetes website on SharePoint

We are pleased to announce the launch of a new SharePoint website for diabetes resources, containing printable handouts for patients and clinical tips/standards of care for providers! We welcome ideas for new resources or corrections/updates to existing resources.

From the SFHN IntraNet home page, click on SharePoint: (UCSF and Consortium providers: access via your active directory login.)

Under ZSFG Intranet, select DiabetesResource in the dropdown menu:

Once you're at the Diabetes Resource Website, save it as your favorite for the future:



Making sense of diabetes medications: What? When? How?

The plethora of diabetes medication classes now available for type 2 diabetes is mind boggling. On the one hand, having a wide range of medication classes to address the multiple defects leading to hyperglycemia allows us to better tailor treatment to each patient. On the other hand, the advent of newer medications has justifiably received scrutiny given the rising costs of diabetes-related health care in the U.S. even as the percentage of people with diabetes achieving A1C targets is not improving (Diabetes Ther). A recent ADA survey showed that total direct costs of diabetes care has doubled from $116 billion in 2007, to $237 billion in 2017, of which 38% were for outpatient medications and supplies. This cost burden is borne not just by the U.S. healthcare system, but on the backs of individuals with diabetes, contributing to nonadherence and discontinuation of prescribed therapies (JAMA).

What can we as providers do? There is a sweet spot (no pun intended!) between tried and true older medications and the judicious use of new medications that can help our patients achieve their A1C goals. The ZSFG Diabetes Team is in the process of updating our oral medication and insulin algorithms, but here are some pearls for clinical practice, focusing on medications for **type 2 diabetes**:

First-line treatment should always start with metformin to counteract hepatic glucose output and reduce insulin resistance. Note new FDA guidelines using eGFR to guide dosing of metformin in those with CKD.

eGFR (ml/min/1.73 m²)	**OK to start metformin?**	**Ok to continue metformin?**
> 45	Yes!	Yes!
30 - 45	Not recommended	Consider dose reduction
< 30	Contraindicated	No

Sulfonylureas are a safe and effective add-on drug to metformin. You may have seen the misleading headline in a recent population-based cohort study from the U.K. published in BMJ concluding that sulfonylureas as second-line drugs are associated with an increased risk of MI, mortality, and severe hypoglycemia compared with remaining on metformin. However, their primary analysis was problematic, grouping together people who switched from metformin to a sulfonylurea (n=9,000) along with those who added a sulfonylurea to metformin (n=13,000). Those who stopped metformin and started a sulfonylurea showed a statistically significant increase in cardiovascular events and, not surprisingly, hypoglycemia. However, those who stayed on metformin and added a sulfonylurea showed absolutely no increased CV risk. While the data is convincing that replacing metformin with a sulfonylurea increases your CV risk, it is unclear if that is due to stopping metformin (a drug with known CV benefit) or starting the sulfonylurea. In addition, the authors' analysis did not account for severe kidney disease and decompensated heart failure (contraindications to metformin) as possible reasons why the sulfonylurea group had more events. Our read of this study: adding a sulfonylurea to metformin does not increase the risk of cardiovascular disease, but replacing metformin with a sulfonylurea might.

In your patients with type 2 diabetes who are not controlled on metformin + sulfonylurea, basal insulin is still our recommended go-to 3rd agent. NPH is a fine choice and significantly less expensive than newer insulin analogs**.** No basal insulin is more efficacious than another in lowering A1C. Basaglar (glargine), manufactured by Lilly, is the newest basal insulin analog that is biosimilar to Lantus (glargine), manufactured by Sanofi. Basaglar is on formulary for SFHP medi-cal, however Lantus remains on formulary for HSF in patients with type 1 diabetes, or type 2 who experience hypoglycemia on NPH. In real-world studies, the incidence of severe hypoglycemia with NPH does not exceed that of the more expensive basal insulin analogues whose clinical trials are generally titrated to achieve very low FBG targets. JAMA recently published a retrospective study of 25,000 Kaiser patients with type 2 diabetes comparing NPH and basal analog insulins between 2002-2013. In real-world use in this Kaiser system, there were no significant differences in hypoglycemia-related ER visits or hospital admissions (with a trend toward fewer with NPH). Additionally, patients on NPH had 0.2% better A1C lowering which was statistically significant though probably not clinically meaningful.

How about newer agents?

- GLP-1 agonists are non-insulin injectables that reduce post-prandial glucoses, help patients lose weight, and do not directly cause hypoglycemia. Daily and weekly **GLP-1 agonists** have been added to formularies for HSF, SFHP medi-cal and Anthem BC medi-cal (as well as many Medicare part D plans). They can be a useful adjunct, usually after treatment failure of metformin and sulfonylurea +/- basal insulin AND if you only need to lower A1C ~1% to get to goal. Among GLP-1s, the FDA has only approved liraglutide (Victoza) to reduce the risk of major cardiovascular events (CV death, non-fatal MI, non-fatal stroke) in adults with type 2 diabetes and established CV disease. A 2-year study of semaglutide (Ozempic) among patients with established CV disease or at least one risk factor showed a significant decrease in the rate of non-fatal stroke, but is not FDA approved for CVD outcomes. The downsides of GLP-1 agonists: they are injectable, cost 4-6x more per month than basal insulin, pose a pancreatitis risk and many patients can't tolerate the nausea. See our updated GLP-1 agonist cheat sheet, also located on our SharePoint site.

- **DPP-4 inhibitors** are mechanistically related to GLP-1 agonists but are weaker and have no effect on weight or CVD. They generally lower A1C ~0.5-0.8%. and are expensive. Perhaps because it is easier to have patients add another pill rather than start insulin, the use of DPP-4 inhibitors has skyrocketed in our system over the past 5 years without an improvement in A1C levels. DPP-4 inhibitors may be useful if your patient is very, very close to goal, but insulin should not be delayed when there is significant hyperglycemia. Thus HSF formulary restricts use of sitagliptin (Januvia) to patients with A1C < 8.5%. SFHP medi-cal prefers alogliptin in this class and we encourage providers, when able, to switch those patients from other DPP-4 inhibitors to aloglipitin.

- **SGLT-2 inhibitors** reduce the kidney's ability to reabsorb glucose, thus releasing more glucose into the urine. Risks include dehydration, UTI, genital mycotic infections and perhaps increased amputations (in canagliflozin only). A1C lowering is modest (< 1%). That said, empagliflozin (Jardiance) has shown

significant cardiovascular benefit and is FDA approved to reduce the risk of CV death in adult patients type 2 diabetes and established CV disease and should be considered in these high risk patients. SGLT-2 inhibitors cost 3x more than basal insulin.

- With any of these agents, if no improvement in A1C is seen after 3-6 months of use, they should be discontinued.

The ZSFG Pharmacy Department has a great updated cheatsheet summarizing formulary options of the most common insurances we see. You can also do more detailed formulary searches online for SFHP medi-cal and Anthem BC medi-cal.

Welcome Diabetes Team's Newest Member

Hi! I'm Bessa Makoni NP and hopefully you've already seen me around. I'm joining the Diabetes Clinic and will also be at RFPC Wednesday nights with a focus on patients with diabetes who need close medication titration and education. I come from 8 years at a community clinic in Fremont where I worked with HIV+ and transgender patients, as well as in primary care. Most importantly, I am the mother of 2 young children ages 1 and 4, who are my bosses at home. I'm so excited to be here and work with so many smart and lovely people.

Diabetes Resource Website:

https://in-dphsp01.in.sfdph.net/sfgh/DMRes/SitePages/Home.aspx

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